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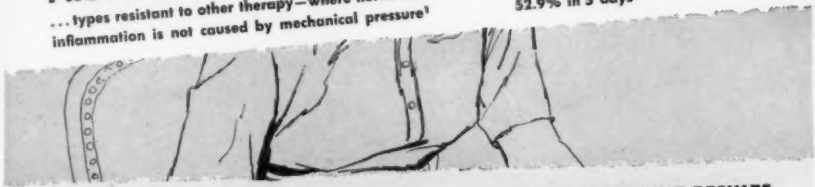

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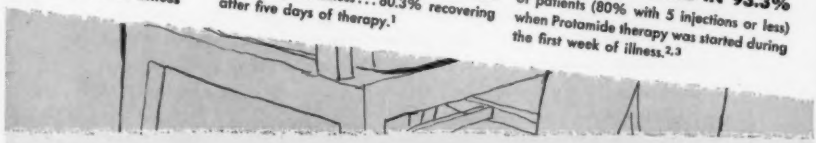

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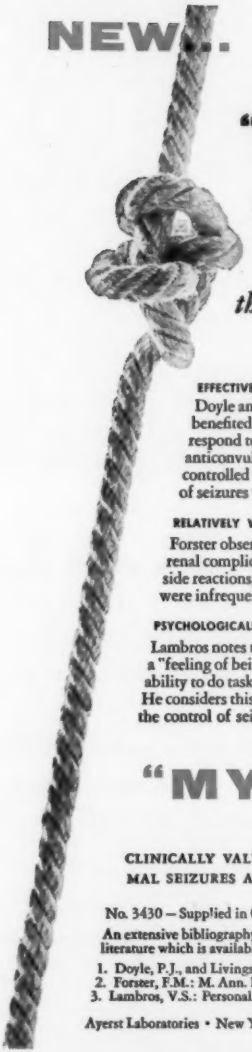

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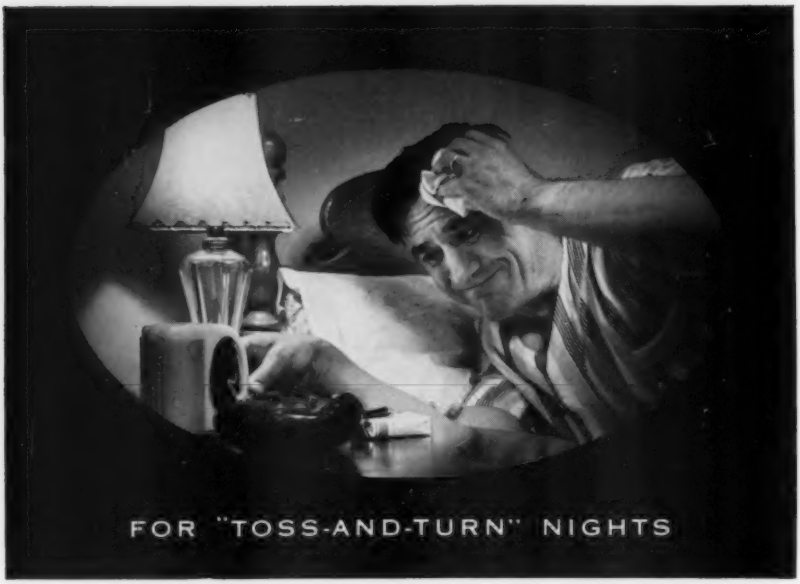

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Contents • SEPTEMBER, 1954

Complications of Cerebral Angiography
ALBERTO D. KAPLAN, M.D. AND A. EARL WALKER, M.D. 643

Effects of Serpasil on Behavior and Autonomic Regulating Mechanisms
JURG A. SCHNEIDER, M.D. AND ALFRED E. EARL, D.V.M. 657

The Status of Neurology as a Specialty in Various Countries
LOTHAR B. KALINOWSKY, M.D. AND H. HOUSTON MERRITT, M.D. 668

Studies on Experimental Concussion
Relation of Physiologic Effect to Time Duration of Intracranial Pressure Increase at Impact
E. S. GURDJIAN, M.D., H. R. LISSNER, J. E. WEBSTER, M.D., F. R. LATTIMER, M.D. AND B. F. HADDAD, M.D. 674

Treatment of Parkinsonism with Pagitane Hydrochloride
ADOLFO ZIER, M.D. AND LEWIS J. DOSHAY, M.D. 682

Treatment Review
Recent Methods of Management of Spinal Cord and Cauda Equina Injuries
BENJAMIN BOSHES, M.D., ISRAEL ZIVIN, M.D. AND ELI L. TIGAY, M.D. . 690

Clinical Pathologic Conference
Presented by HELENA E. RIGGS, M.D. AND CHARLES RUPP, M.D. 705

(Continued on next page)

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Contents — *Continued*

Case Reports

Tuberculous Spondylitis Simulating Herniated Intervertebral Disk
HAROLD BERRIS, M.D. 710

Coccidioidomycosis of the Central Nervous System
DAVID D. NORMAN, M.D. AND ZONDAL R. MILLER, M.D. 713

Total Left Cerebral Hemispherectomy for Malignant Glioma
WILLIAM F. HILLIER, JR., M.D. 718

Book Reviews 722

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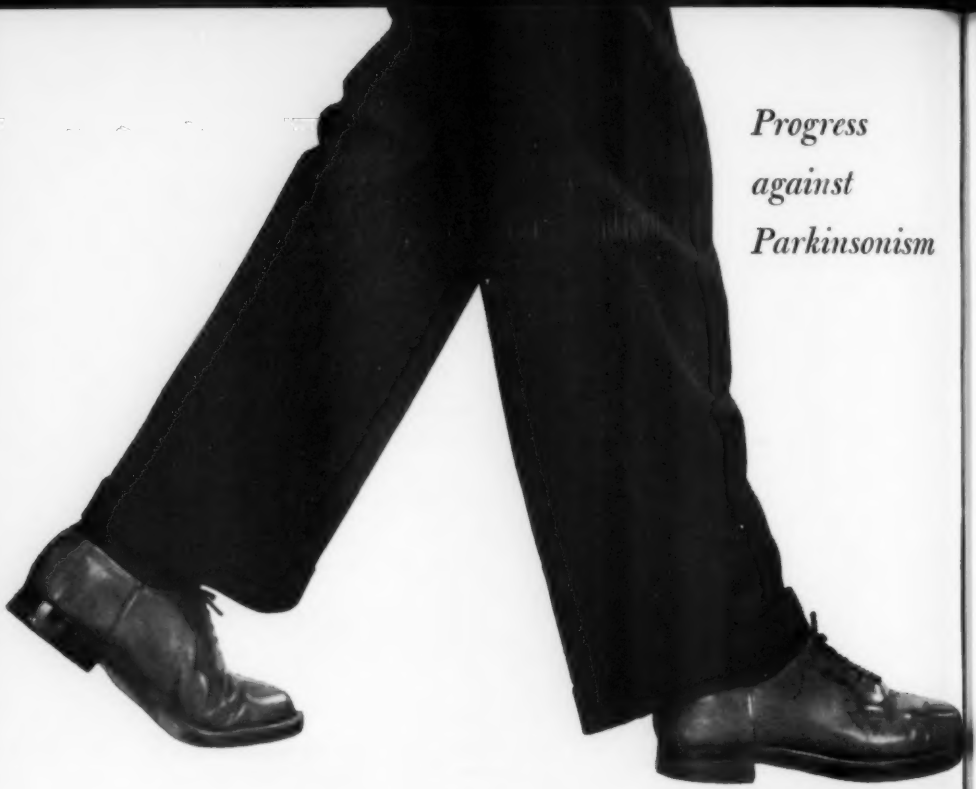

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Neurology

Complications of Cerebral Angiography

Alberto D. Kaplan, M.D. and A. Earl Walker, M.D.

At the present time cerebral angiography gives the neurosurgeon more pertinent information regarding intracranial lesions than any of the special diagnostic tests, yet there has been a certain reserve on the part of both neurologists and neurosurgeons to use this procedure. This hesitation stems from the recognized complications which loom large, especially in the minds of those unacquainted with the advantages of the technic. On the other hand, diagnosticians employing the procedure routinely are willing to accept the calculated risk for the unique information obtained, which greatly aids in subsequent surgical treatment of the case. A minor complication rate of 3 to 4 per cent may be quite justifiable if a major complication rate can be lowered significantly. Admittedly the difficulties encountered in any diagnostic test will depend not only on the inherent shortcomings, but also on the experience with the procedure and the use made of the technic. Hence if angiography is employed only rarely and as a last resort, often on a moribund patient, the complications will be high. Therefore it is not justifiable to assume that the complications reported in the literature in small series of cases represent the usual experience with angiography.

This report comes from a hospital in which angiography is done routinely as a diagnostic procedure, when other technics have failed to establish a definite diagnosis or have proved a condition requiring surgical intervention. Accordingly the technic of angiography is fairly well standardized and the team carrying out the procedure is highly skilled.

From the division of neurological surgery, The Johns Hopkins University School of Medicine, Baltimore.

Read at the sixth annual meeting of the American Academy of Neurology, Washington, D. C., April 30, 1954.

MATERIAL AND METHODS

Five hundred consecutive cerebral angiograms, performed at The Johns Hopkins Hospital between February 1951 and April 1953, were reviewed to determine untoward reactions. These procedures were carried out on 484 patients representing the usual neurosurgical population in a general hospital, distributed as follows:

Abscess, brain	6	Hematoma, subdural	8
Aneurysm, ruptured	25	Hemorrhage, intracerebral	6
Aneurysm, unruptured	11	Sclerosis, multiple	8
Aneurysm, suspect (subarachnoid hemorrhage)	22	Syphilis, central nervous system	15
Arteriosclerosis, cerebral	48	Trauma, head	29
Atrophy, optic	21	Tumor, brain verified	97
Cephalalgia	27	Tumor, brain suspect	20
Epilepsy	84	Miscellaneous	29
		Undiagnosed	28

The sex incidence was essentially equal, with 248 males and 236 females comprising the series. There were 105 colored patients in the series. However, since neither sex nor race seemed to play a role in the incidence of complications, these factors will not be considered further.

The age distribution is approximately that of the usual hospital population, but the details are given in the consideration of factors influencing complications. Complicating systemic disease was present in a certain number of cases, and its relation to complications will be discussed later in this presentation.

Cerebral angiography was carried out under local infiltration anesthesia (1 per cent procaine) except in patients under the age of 12 and in some 15 uncooperative adults. General anesthesia (ether or Pentothal) with an intratracheal tube in place was used for these cases.

In all instances sensitivity to Diodrast was checked by a conjunctival test performed 30 to 45 minutes before the injection. In no instance in this series was the test interpreted as positive, even in patients who had had previous angiography with the same contrast medium.

Direct percutaneous puncture of the carotid (491 cases) and vertebral arteries (eight cases) was made; in one patient, a child one year of age, the carotid artery was exposed in the neck and the arteriogram performed under direct visualization. The artery was punctured with a No. 18 very sharp (often sharpened with a hone at the time of angiography) needle or in children with a No. 19 needle. The needle was connected to a syringe so that a constant stream of saline could be injected in the artery between injections of the dye.

Diodrast (35 per cent) was used in all but one case. In this case a retrograde injection of the carotid artery was performed with 52.5 per cent Diodrast. The total amount injected varied from 30 to 90 cc. in adults and from 10 to 30 cc. in children under the age of 12. The amount used in single injections varied from 10 to 15 cc. in adults and from 5 to 8 cc. in children. Lateral and anteroposterior stereoscopic views were taken in the majority of

cases to show arterial, capillary, and venous phases of the cerebral circulation. Ordinarily 12 films were exposed in the course of making the serial angiograms.

During injections, the patient usually complained of pain at or near the site of injection, burning pain and flushing in the ipsilateral side of the head.

In four patients, bilateral carotid arteriograms were performed at the same sitting without ensuing complications.

The procedures were carried out by five different house officers using similar technics. The incidence of complications was essentially the same for each operator.

CLINICAL COMPLICATIONS

In this series of 484 patients having 500 angiograms, 36 patients had complications to the procedure or died (17 patients) before leaving the hospital. By including all such cases in this analysis we are endeavoring to meet the possible criticism that a subjective bias might be operative in the selection of cases having complications. If all of these patients are considered to have

TABLE 1

COMPLICATIONS OF CEREBRAL ANGIOGRAPHY IN THE DIFFERENT DIAGNOSTIC GROUPS

Diagnosis	*Number of cases*	*Complications*		*Total*
Aneurysm, ruptured suspect	47	2 D 2 HSP	2 P C	7
Arteriosclerosis, cerebral	48	HAP AP	C V B	5
Cephalalgia	27	U	N	2
Epilepsy	84	U	N	2
Hematoma, subdural	8	HA		1
Hemianopsia	3	P		1
Hemorrhage, intracerebral	6	D		1
Meningitis, tuberculous	1	D	*	1
Tumor brain, suspect	20	A		1
Tumor brain, verified	97	HA C	†	2
Total number of complications		Death ..... 4 Motor and sensory ..... 10 Convulsions ..... 3 Visual disturbances ..... 2 Urticaria ..... 2 Hematoma of the neck 2		23

*One day after angiography, convulsions occurred and the patient died within an hour.

†One patient in this group might be said to have had a visual complication. One hour after angiography she noted zig-zag lines in the central fields, for a few minutes.

A—Aphasia
B—Blindness followed by visual agnosia
C—Convulsions
D—Death
H—Hemiplegia
N—Hematoma of the neck
P—Paresthesias
S—Sensory loss
V—Central scotoma

had untoward reactions to angiography, and we do not believe this to be the case, the maximum complication rate would be 7.2 per cent, with an over all mortality of 3.4 per cent. But we believe that 13 of the deaths were unrelated to angiography, but were the result of the primary disease for which angiography was performed. Several died more than a month after the diagnostic procedure and eight had surgical procedures for brain tumor, abscess, subdural hematomas, or intracerebral aneurysm at some time after angiography. There were nine patients in this series, who were admitted in coma due to intracerebral bleeding on whom emergency angiograms were done, and who remained unchanged in coma and eventually died after the procedure. In these 13 patients, we believe that angiography played no role in their demise, and that they should not be included in the complications of this series. This would give a corrected mortality of 0.8 per cent and a complication rate of 4.6 per cent. In the remainder of this discussion these corrected mortality and morbidity figures will be used for the incidence of complications in this series.

Local complications. The trauma of the needle passing through the vessel wall gives rise to surprisingly few clinical sequelae, although there is unquestionable local reaction. Occasionally, however, it seems probable that emboli from the site of puncture have reached the intracerebral and retinal vessels causing infarction. Larger clots may produce a complete thrombosis of the internal carotid artery, as reported by Dunsmore and co-workers.[23] Rarely the needle may fail to penetrate the intima and the dye may cause a dissection of the lining of the vessel. Sirois and Lapointe[56] reported a case in which dye did not reach the cerebral vessels, and at autopsy the intima was found peeled from the muscular coats causing a valvular obstruction of the artery.

Perhaps trauma is done to periarterial structures more commonly by misdirected punctures or bleeding into the tissues. In 1944 Engeset[27] reported a transient Horner's syndrome after angiography. A similar complication lasting four weeks was mentioned by Wilkinson and co-workers.[70] These angiograms were made by percutaneous puncture, but the complication may develop with the open technic. Picaza[50] presented three such cases in which the Horner's syndrome cleared within eight weeks. Injuries to the sympathetic chain have also been reported.[1,23] Transient pupillary dilatation has been observed by Falls and co-workers.[28] We have also noted this phenomenon, but its relationship to irritation of the sympathetic chain is not certain. Vocal cord paralysis has also resulted from the trauma of angiography, fortunately being only a temporary disturbance.[1,16,25,41] The roots of the brachial plexus may be injured by the needle or bleeding, as reported by Abbott and co-workers.[1] This occurred in one case of our series. Fink and Stein[29] reported an osteomyelitis of the fifth cervical transverse process following angiography. Two patients mentioned by Picaza[50] developed pneumomediastinum after carotid angiography.

Not only may bleeding into the tissues of the neck cause irritative effects, but the bulk of the clot may also cause compression of the trachea or larynx.

In two of our cases large hematomas formed in the neck produced discomfort but fortunately no obstruction of the airway. Other writers have reported more serious hematomas requiring intubation.[29] Some bleeding into the neck has been mentioned by several authors.[1,22,41,62,70] Ecker[25] believed laryngeal spasm was due to local trauma in the neck. In some series suggilation of the larynx has been a rather common complication,[4,62] but Olson[46] thought laryngeal edema was attributable to an allergic reaction to the dye rather than trauma.

Hemiplegia. Hemiplegia associated with paresthesias, aphasia, and/or sensory changes following angiography with 35 per cent Diodrast probably occurs in from 2 to 10 per cent of cases. In our series motor or sensory disturbances resulted in ten cases. All but one cleared within a period from 24 to 48 hours after angiography. The exception was one patient with pre-existing aphasia whose exacerbation merely regressed to his previous state within 24 hours. The hemiplegic state may remain permanently in some degree, and the literature indicates that such a condition prevails in somewhat less than 20 per cent of the cases suffering this complication.

Many writers have reported hemiplegia with or without aphasia and sensory changes as a complication of angiography. In Fink and Stein's[29] series of 117 cases, seven patients developed a temporary hemiparesis or aggravation of the pre-existing weakness. In one case hemiplegia was permanent; another patient developed a persistent aphasia.

Of 526 angiograms reviewed by Rowbotham and associates,[54] 30 were followed by hemiplegia which was permanent in 12 cases and transient in 18. Dysphasia occurred in 14 patients and mental confusion in ten.

In the series of 234 consecutive arteriograms reported by Perese and co-workers[49] permanent hemiplegia developed in three patients suffering from subarachnoid hemorrhage; transient hemiplegias were observed 19 times in six patients with brain tumors, nine arteriovenous or berry aneurysms, two subdural hematomas, one brain contusion, and one epilepsy. A transient contralateral sensory impairment occurred in six other patients.

Although angiography is frequently performed shortly after a subarachnoid hemorrhage, few reports have been made of its precipitating a bleeding. Stein and Fink[58] had one such case, a patient with a vascular anomaly who developed subarachnoid hemorrhage after an angiogram.

Mental confusion. Mental confusion associated with other complications such as hemiplegia usually clears with the other sequelae, but occasionally it has been reported to progress to coma and death. Wise and co-workers,[71] Lindgren,[44] and Olsson[45,46] have reported cases in which mental confusion cleared up within 12 to 36 hours. Coma with subsequent recovery has been mentioned by Idborhn[38] and by Falls and co-workers.[28] We have had no experience with this complication.

Brain stem involvement. Vertebral angiography is apt to be complicated by vascular involvement of the brain stem. Abbott and co-workers[1] reported transient attacks of decerebrate rigidity in one patient after vertebral angi-

ography. Radner[52] also observed such complications. One case was a 30 year old woman having vertebral angiography performed by catheterization with 40 cc. of 35 per cent Umbradil. The following day she had ptosis of the right eyelid, miosis, right cerebellar signs, and deviation of the uvula to the left. These signs improved within three weeks. In another patient with a basilar aneurysm, weakness of both arms developed ten minutes after angiography, followed by coma, respiratory embarrassment, and death in two weeks.

Convulsions. With high concentrations of Diodrast for angiography seizures are a common occurrence,[34,35,36,37,27,43] but with a 35 per cent solution of the dye the incidence is approximately 1 per cent. Often the patient is found to have had convulsions previously. In four of the patients in this series convulsions occurred after the injection of Diodrast. In two cases the patients were known to be subject to seizures; one patient had had attacks due to a meningioma and the other had had focal seizures in association with cerebrovascular disease. In another case seizures occurred 24 hours after the injection and, since the patient had tuberculous meningitis, one might wonder if the two events were etiologically related. Convulsions, both focal and general, may complicate angiography and have been reported by practically everyone writing on the subject.

Visual disturbances. Two cases in this series developed visual disturbances after angiography. One of them (previously reported by Otenasek and Markham[47] and Walsh and Smith[66]) about two hours after the injection developed impaired vision in the right eye, which was shown to be due to a large right central scotoma. The vision returned to normal within 48 hours. The second case was that of a presumed thrombosis of the left posterior inferior cerebellar artery. After the second injection of 8 cc. of 35 per cent Diodrast into the left vertebral artery the patient developed bilateral blindness, confusion, and dysarthria. The following morning he was found to have weakness of all four extremities, to be more confused, and to have frequent and annoying hiccoughing. After four days his condition began to improve and a month later his vision had regained its previous acuity, but he still had a visual agnosia and weakness of all four extremities. One year later the only abnormality was visual agnosia.

Visual disturbances have been reported not infrequently. The abnormality is usually in the eye on the side of the angiography and may take the form of a scotoma,[28] quadrantic defect,[19,68] hemianopsia or complete blindness of within a few hours or days, but it may be permanent in varying degrees of one or both eyes.[28,44,66] In most cases the condition is temporary, clearing severity.[19,60,62] Homolateral changes have been attributed to embolism or spasm of the retinal artery. Falls and co-workers[28] believe that ocular complications are very frequent, but must be looked for carefully. Petechial hemorrhages in the skin, conjunctiva, and retina may be found upon scrutiny. Visual complications following vertebral angiography, especially blindness, are not uncommon. Rozanski[55] described one case of visual hallucinosis lasting two weeks, which consisted of colorful geometric patterns and landscapes.

General or systemic reactions. There is probably a general reaction to angiography but it rarely is sufficiently severe to be of clinical significance. A mild fever is common but lasts no more than one to three days. Olsson[46] noted its occurrence in 16 of 330 cases.

Allergic reactions are rare and, although all patients were tested for sensitivity by a conjunctival instillation,[2] only one of our patients gave a positive reaction. Fifteen patients gave a history of some form of allergy but none had a reaction. However, two patients had urticaria, although they had no history of allergy.

Pendergrass and associates[48] found ten deaths within 24 hours and 26 deaths within 25 days in a survey of 661,800 patients receiving intravenous injections of Diodrast. The former were presumably allergic reactions. Such accidents do not seem to occur following angiography with Diodrast. Allergic reactions reported in the literature have been rather mild and urticaria is its most common manifestation.[23,25,29,33,41,45,46,59,70]

Ecker[25] described an allergic syndrome of trismus and lingual obstruction of the airway occurring five to 30 minutes after the completion of angiography. Although this has caused no fatalities in carotid angiography, death might follow if adequate measures to reestablish the patency of the airway were not taken.

Death. A fatality following angiography has not been too rare an occurrence. In most instances the question has been raised regarding the etiologic role of carotid injection in the mortality, for most of the deaths have occurred in patients suffering from severe intracranial conditions (aneurysms, brain tumors, and so on) and not a few cases were comatose or moribund at the time of angiography. For this reason it has been difficult to assess the risk of the procedure. There is no doubt that it does carry a definite hazard to the life of the patient.[20,51,52,54,62]

In cases of brain tumors, Diodrast may increase intracranial pressure by causing a cerebral edema, producing increasing herniation of the brain through the tentorium or the foramen magnum. In cases of vascular disease,[19,23,25] the patient may suffer additional thromboses or hemorrhages in the brain substance. In other cases, death has resulted from pneumonia secondary to a hemiplegia. But in some instances the cause of death is not readily ascertainable, and perhaps should be attributed to contributory factors such as the primary disease and the reaction to Diodrast.

In this series four patients (0.8 per cent) apparently succumbed as the result of angiography.

Case 1.—A 51 year old woman, who had been complaining of right parietal headaches for six weeks, had a sudden exacerbation of the pain followed by loss of consciousness lasting a few minutes on September 25, 1951. Upon admission to the hospital the patient was alert and cooperative and had no abnormal neurologic findings except stiffness of the neck. Her blood pressure was 270/110. On lumbar puncture the cerebrospinal fluid was bloody and under increased pressure. A right carotid angiogram was performed under local anesthesia on September 29, and four injections of 15 cc. each of 52.5 per cent Diodrast were made using a retrograde technic. Only the external carotid artery was visualized. Im-

mediately after the last injection the patient became comatose and developed a left-sided hemiplegia. She was restless and confused until her death four days later. Permission for autopsy was not obtained.

Case 2.—A 52 year old colored man, who had suffered headaches for several weeks previously, was found unconscious in his room. Upon hospital admission November 24, 1952, he was comatose, had bilateral dilated pupils, spasticity of both lower extremities, and flaccidity of the right arm. His blood pressure was 195/100. The spinal fluid, under a pressure of 600 mm., was turbid and pink. The same day a left carotid angiogram was made with four injections each of 12 cc. of 35 per cent Diodrast. The anterior cerebral artery was shifted to the right side. Five minutes after angiography the patient stopped breathing; a large left parietotemporal intracerebral hematoma was found at autopsy.

Case 3.—A 44 year old colored woman developed inappropriate laughter, mental confusion, and convulsions on April 4, 1952. When examined she was confused, her neck was stiff, and her eyes deviated to the left side. The right extremities were moderately rigid. Her blood pressure was 220/120. On lumbar puncture the cerebrospinal fluid was bloody and under a pressure of 210 mm. of spinal fluid. A left carotid angiogram was attempted shortly after admission, but the lateral films were not satisfactory. During the procedure the patient had several convulsions which stopped after 320 mg. phenobarbital was injected into the carotid artery. Gradually she became less responsive and finally died two hours after angiography. Permission for autopsy was not granted.

Case 4.—A 46 year old colored man, who had begun to develop a left hemiparesis three years previously, experienced lethargy, increased left sided weakness, and headaches in the first week in November 1952. He was found to have a left sixth nerve palsy, weakness, hyperactive deep tendon reflexes, and a right positive Babinski. His blood pressure was 136/98. On lumbar puncture the fluid was cloudy but under normal pressure. It contained 400 mononuclear cells and a total protein of 108 mg. per cent. A right carotid angiogram was performed and interpreted as normal, but shortly after the last injection the patient became drowsy and his eyes deviated to the right. He developed left-sided convulsions during the following day and died 24 hours after angiography. An autopsy was not done. Cultures of the cerebrospinal fluid were reported positive for tubercle bacilli.

FACTORS INFLUENCING INCIDENCE OF COMPLICATIONS

Biologic factors. The sex and race of the individual undergoing angiography does not seem to play a significant role, but the age of the patient does influence the likelihood of complications. In patients over 50 years of age, complications of all types appear to be more frequent than in younger patients; in fact in this series they were about twice as frequent. In all probability this increased vulnerability is simply a reflection of the decreased resistance of older people. But there may be the added factor of a greater incidence of vascular disease in this age group, for this condition does seem to predispose to complications, perhaps by decreasing the total amount of blood passing through the brain as well as slowing the cerebral circulation.[45]

The primary condition. Early in our experience it was suggested that complications rarely occurred in patients with brain tumors, but are not uncommon in patients without a discernible organic cerebral lesion. This conclusion is unjustified, but it is true that the disease for which the angiogram is performed is a factor in the likelihood of complications. Vascular disease is associated with a much higher incidence of complications than neoplastic or convulsive disorders. This is true irrespective of whether the vascular disease is

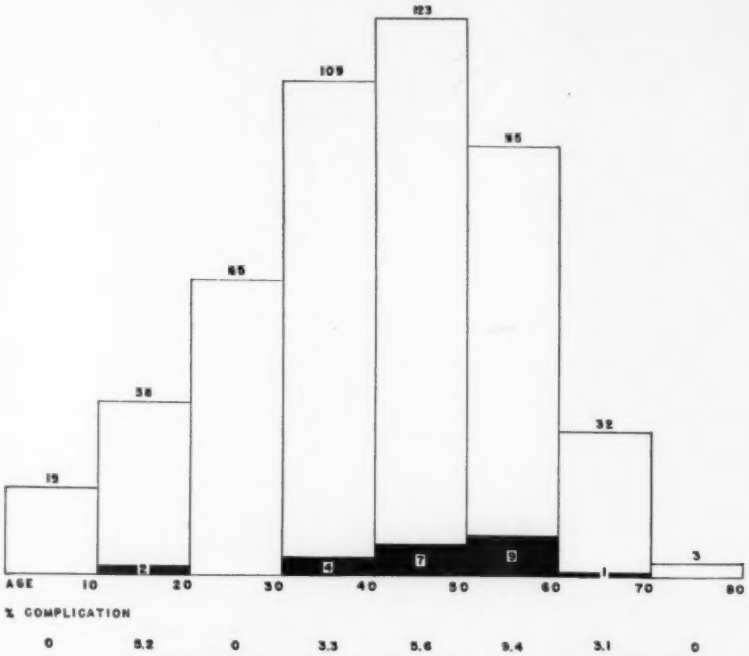

FIG. 1. Incidence of complications following cerebral angiography in the different age groups.

the primary condition or merely a secondary complicating factor. In this series patients with a systolic blood pressure greater than 160 mm. Hg represented 12 per cent of the complications whereas those with a normal blood pressure represented only 3.7 per cent.

The cerebral circulation. Any factors tending to decrease the rate of the vascular circulation appear to increase the incidence of complications.[3,5,6,12,13] In this series some patients appeared to have a slow circulation as determined by the amount of dye in the intracranial vessels at two and four seconds after injection. These constituted 17.3 per cent of the patients having complications and none occurred in patients without complications. With a normal circulation time the dye is within the cerebral vessels in two seconds and in the veins at four seconds. The factors causing a slowing of the flow are not clear. Presumably vascular spasm[26] of the internal carotid artery (two cases in this series of complications) could induce this state, and certainly atherosclerosis would do so. But we suspect that other conditions may be responsible at times.

The time of angiography. Despite reports to the contrary, we believe that angiography within hours of a cerebral accident has a greater risk than one performed after the initial shock has passed.[26] We suspect, again without

actual proof, that the primary insult is associated with a degree of vascular spasm which slows the cerebral circulation, thus allowing the dye greater time[12,13] for its local effect on capillary walls and neurones. Thus we favor waiting nine or ten days after rupture of a cerebral aneurysm before carrying out angiography, unless the presence of an intracerebral hematoma is strongly suspected. The mortality of this condition is so high (80 per cent) that early operative interference is warranted. Since angiography may give invaluable information to the surgeon in such cases, a certain calculated mortality seems justified. But if a patient is progressing satisfactorily after a subarachnoid hemorrhage, with perhaps the use of hypotensive drugs, we would favor waiting seven to ten days before angiography and operative interference.

PATHOGENESIS OF COMPLICATIONS

The mechanisms producing complications after angiography have been the subject of considerable investigation, with not entirely unanimous conclusions.

Vasospasm. Vascular spasm[26,64,67] has been assumed to be a cause of neurologic deficits following angiography for many years, but many investigators have not been able to convince themselves that such a phenomenon actually occurs within the cerebral vessels. Certainly it is seen in the carotid artery but doubt has been cast upon its presence in the cerebral arteries, although some investigators believe they have seen it in experimental animals. In our experience, with microscopic examination of the pial vessels during angiography, it has not been definitely seen in many observations.[13]

Increased capillary permeability. Experimental studies of Browman[7–12] and others[3,5,6] have emphasized that Diodrast in higher concentrations does cause an increased vascular permeability as determined by passage of dye through the blood-brain barrier.[31,40] This occurs with the higher concentrations of Diodrast according to Smith and co-workers,[57] and with certain samples (presumably more toxic) of Diodrast. Even with relatively large amounts of 35 per cent Diodrast, no changes in the vascular permeability may be noted.[11,12,17,18,45,46]

Irritation of neurones. A number of investigators have shown that there are electroencephalographic changes during the passage of Diodrast through the brain.[5,6,30] This is assumed to be due to the toxic effect of Diodrast on neurones as the result of its passage through the blood-brain barrier.

Emboli. The suspicion has been voiced occasionally that hematogenic and air emboli may play a role in the complications of angiography.[3] As we have emphasized previously,[65] although the actual embolus may be of no clinical importance, the fact that it slows the cerebral circulation in an area and allows the toxic concentrated agent to act on the capillary wall for minutes to hours may be of great significance. Such a long period of contact may well be responsible for both changes in capillary permeability and neuronal irritation.

Allergy. Pure allergy seems to be a very rare cause of complications.[32,42,53] It is estimated that sensitivity to Diodrast and other iodine compounds is present in approximately one out of 8,500 people.[48]

Technical complications. Factors related to the technical procedure may be responsible for complications. Difficulty in entering the artery, perhaps due to a blunt needle, may necessitate multiple punctures with resulting trauma to cervical structures and perhaps bleeding. If the procedure is carried out under anesthesia[25] complications inherent in the anesthesia may occur, such as laryngeal spasm, heart arrest, and so on. Moreover the anesthesia may mask a complication of the procedure, so that it is either not recognized or recognized late. Occasionally under anesthesia a nerve root may be traumatized while endeavoring to cannulate the artery and may cause a transient neuritis, a complication in one case in this series.

PROPHYLAXIS

Complications of angiography may be prevented by careful attention to the selection of cases and the technic of the procedure. We believe it is unwise to subject a moribund patient to angiography when there is no chance that the patient could survive a surgical procedure if a condition amenable to an operation were demonstrated. It would seem advisable to treat the patient conservatively until such time as his condition improves. For example, the patient comatose from a subarachnoid hemorrhage is a poor risk for the first seven to ten days, and should not be operated upon until that period of time has elapsed since the rupture. Accordingly, there is no rationale for an emergency angiogram when operation is not contemplated. It seems probable, although the evidence is not too clear on this point, that the final mortality from subarachnoid hemorrhage will be less if patients are not subjected to angiography or operation early.

Acute anaphylactic shock may be avoided by the routine testing[48] of patients, but unfortunately only a small proportion of the complications may be prevented by this technic. In the event of sensitivity, Thorotrast may be used in place of Diodrast for angiography.

There is little good evidence that prophylactic drug therapy is effective. Papaverine, a vasodilator, has been advocated but no convincing figures of its value have been presented. Blocking of the cervical sympathetic ganglia is not effective in the prevention of vasospasm. It might be argued that vasoconstriction might be beneficial, since it prevents large amounts of the dye reaching the arterioles and capillaries.[30]

Care in the actual puncture or injection of dye may prevent air and blood emboli. If dye is not seen in the intracranial vessels on the first films taken, it is wise not to make further injections for the likelihood of complications is great. At a later time the angiogram may be repeated without such difficulties, or some other diagnostic technic may be employed.

The actual technic of carotid puncture may be greatly simplified if the patient is adequately sedated and anxiety allayed. The barbiturates may serve two purposes, to decrease nervousness and to inhibit convulsions. Phenobarbital may be desirable for these purposes.

TREATMENT OF COMPLICATIONS

Local complications at the site of injection rarely require active therapy. Occasionally a large hematoma obstructing respiration will require intubation and surgical evacuation. Ordinarily compression of the site of puncture is sufficient to control bleeding.

For the treatment of intracranial complications, more energetic steps are necessary. We believe that immediate procaine injection of the cervical sympathetic ganglia is a useful procedure, producing dramatic improvement in the hemiplegic phenomena in some cases. Repeated injections may be required at times. However, in some cases this form of therapy is ineffective. Intravenous papaverine may be useful in relieving spasm. To increase intracranial circulation the inhalation of carbon dioxide offers the greatest promise. Other vasodilators such as nicotinic acid and amyl nitrite are not particularly effective. If there is absence of pulsation of the carotid artery in the neck, an exposure of the vessel for removal of a clot may be advisable. If treatment is to be effective it must be both immediate and energetic; if delayed the final result is apt to be disastrous. A permanent complication is certainly discouraging to the operator and devastating to the patient.

SUMMARY

In 500 consecutive angiograms, a total of 36 (7.2 per cent) patients died before leaving the hospital or had definite clinical reactions to the procedure. Of the 17 patients who died, we doubt that angiography was etiologically related to the demise in 13 instances; accordingly the corrected morbidity would be 4.6 per cent and mortality 0.8 per cent.

Hemiplegia, paresthesias, or aphasia followed or became temporarily more severe in ten cases. Convulsions occurred in four, visual disturbances in two, urticaria in two, and clinically significant neck hematoma in two.

Although some of these complications are probably due to the inherent toxicity of the drug on vascular tissue, some may be preventable by care at the time of arterial puncture.

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The maladies commonly known by the names of Megrim, Sick-headache, Blind-headache, Bilious-headache, and some others, form a natural group or family of disorders which has not received adequate recognition in our nosologies, although such names as Hemicrania, Cephalalgia biliosa, Suffusio dimidians, and the like, correspond with or include them more or less perfectly.

The popular names recognize some of their most important features—namely, headache of a very intense kind, which is, perhaps, the most constant character of the group, while "Sick" and "Blind" indicate the special features of a certain proportion of them; and "Bilious" points to a theory of their causation, which, as we shall see in due course, carries us back to the days when the ancient humoral pathology still prevailed.

I think, however, that the vernacular *Megrim*, which is of great antiquity, and has an equivalent in most European languages—the Migraine of the French, and *Migräne* of Germans—has acquired by conventional usage a meaning more nearly comprehensive of the whole group than any other. The word itself, as is well known, is a mere medieval corruption of the Greek *Hemicrania*.

Edward Liveing in *On Megrim, Sick-Headache, and Some Allied Disorders,* published in 1873.

Effects of Serpasil on Behavior and Autonomic Regulating Mechanisms

Jurg A. Schneider, M.D. and Alfred E. Earl, D.V.M.

THE ROOT of Rauwolfia Serpentina Benth, a shrub growing in humid areas of India, has been used as a remedy against various kinds of ailments in that country since ancient times. Only in recent years has a systematic and objective scientific investigation of the drug been started. Thus it has been used to combat states of anxiety and excitement.[1,2] Indian pharmacologists[3] demonstrated a hypotensive effect of Rauwolfia in animals, and clinical investigators have confirmed this effect in hypertensive patients.[4–6]

However, the beneficial effects could not be attributed to a single alkaloid. Ajmaline, serpentine, and serpentinine were prepared for the first time by the Indian chemists Siddiqui and Siddiqui,[7–9] and further investigated by Mukherji, Robinson, and Schlittler[10] and Schlittler, Schwarz, and Bader.[11] These compounds did not show sedative hypnotic activity characteristic of the total extract.[12,13]

An active principle of the Rauwolfia root in crystalline form was identified by Müller, Schlittler, and Bein.[14] This step was a major advance in the complicated chemical and pharmacologic problem. The new alkaloid was assigned the generic name of reserpine and is produced under the trade name of Serpasil. Data on its chemical constitution have been published recently.[15] Its basic pharmacologic action has been described as consisting of a sedative hypnotic effect, a hypotensive effect, miosis, increased peristalsis, and lowering of body temperature.[16]

Cardiovascular effects of the drug have also been studied in detail.[17,18,19] The general pharmacology has been reported,[20,21] and the central effects of Serpasil characterized with special regard to antagonizing and synergizing factors in mice.[22]

These authors concluded from their studies that the drug probably acts directly on the autonomic centers of the brain stem, the most likely effect being a suppression of the higher sympathetic centers in the hypothalamic area.

Sleep induced by commonly used sedatives is distinctly different from

With the technical assistance of R. Dibble, E. Holden, and R. Rinehart.

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the so-called sedative hypnotic effect after Serpasil.[22] Doses of the drug which are otherwise pharmacologically active in unanesthetized laboratory animals are always associated with certain alterations in behavior. In this study the effects of chronic and acute administration have been observed in monkeys, with emphasis on the behavioral changes induced by the drug.

MATERIALS AND METHODS

Twelve jungle born Macaca mulatta monkeys were used in 90 experiments. In order to observe the long term effects of Serpasil, four monkeys were studied during a six month period of chronic oral administration of the drug. Observations of the behavior of the animals were carried out with the monkeys confined to a circular table by a short chain so that uncaged animals could be observed very closely. The effects of Serpasil on behavior have been recorded on colored film and compared to those of sodium pentobarbital.

For electroencephalographic experiments the animals were usually placed in a special animal chair. A neck yoke was used to prevent excessive movements of the head and at the same time to keep the monkey from touching his head with his hands. During recordings it was necessary to immobilize the head by an additional head clamp, and the extremities were tied to the chair. Recordings were taken with a Medcraft eight channel electroencephalograph. Needle electrodes were inserted into the skin of the shaved scalp of the monkeys on both sides of the head about 1.5 cm. lateral to the midline in the frontal (1.5 cm. behind the supraorbital ridge), occipital (1.5 cm. in front of the external occipital protuberance), and parietal positions. As a rule the following leads were taken: Left frontal–left parietal (LF-LP); Left frontal–left occipital (LF-LO); Right frontal–right parietal (RF-RP); Right frontal–right occipital (RF-RO); Left frontal–right frontal (LF-RF); Left occipital–right occipital (LO-RO); Left parietal–right parietal (LP-RP).

Animals were observed closely during recording in order to eliminate artefacts originating from spontaneous movements such as blinking. Electroencephalographic and electrocardiographic records of 2 to 10 minutes duration were taken at intervals.

Rectal temperatures were taken during these experiments with an ordinary rectal thermometer or with a Foxborow recording device. Room temperature was recorded continuously.

Systolic blood pressure was measured with an infant cuff placed around the upper arm. Respiratory rate and heart rate were recorded simultaneously. The diameter of the pupil was estimated during the course of the experiment.

Serpasil was given either intravenously or orally via stomach tube.

RESULTS

ACTION OF SINGLE DOSES OF SERPASIL

Doses up to 0.1 mg./kg. intravenously did not elicit measurable responses. Doses from 0.5 to 1 mg./kg. intravenously and 25 to 50 mg./kg. orally consistently produced a typical picture of drug action. The first signs appeared

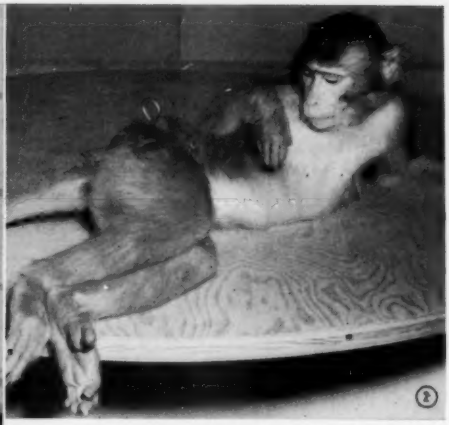

FIG. 1. Rhesus monkey fastened to a circular table. The animal shows the typical excited, aggressive attitude of a jungle-born animal.

FIG. 2. Same monkey as in figure 1 after intravenous dose of 1.0 mg./kg. of Serpasil. Note the relaxed and calm attitude as compared to the behavior demonstrated in figure 1.

30 to 40 minutes after oral or intravenous administration of the drug. Maximum effects were noted approximately two hours after medication, regardless of route of administration. The effects lasted for 12 to 24 hours or longer. When the drug was repeated within a period of seven days, the onset of drug activity was more rapid and produced by smaller doses (0.1 to 0.5 mg./kg. intravenously).

Effects on Behavior

Normal untreated animals behaved in a manner typical of a jungle-born rhesus monkey. They were distrustful of man and constantly sought escape from their environment. Being extremely active and hostile (figure 1), they could be handled with comparative safety only by a person wearing heavy gloves.

Within 45 minutes after intravenous administration of single doses of Serpasil (0.5 mg./kg. to 1 mg./kg.) the monkeys responded in a definite pattern. Initial signs were unmistakable lessening of hostility and resistance to being handled, sometimes preceded by transient excitation. An attitude of apparent curiosity relative to their environment supplanted that of apprehension. The animals became calm and relaxed to a point where some of them were actually playful and assumed a recumbent position typical of complete relaxation. In their relaxed state, the animals might have their eyes opened or closed but no involuntary sleep was induced. Such a monkey could be handled with bare hands without the usual methods of restraint. When phys-

ically molested, little antagonism was manifested. A moderate aggressive attitude could be induced but only after a relative high degree of provocation.

As the degree of drug effect increased the monkeys became less active. They assumed a sitting or recumbent position (figure 2) with the head lowered, and remained in such positions without restraint for indefinite periods unless disturbed. When aroused the animals responded with a coordinated pattern of activity. However, the intensity of such responses was reduced. The quiescent state was reassumed when disturbing stimuli were removed. At this stage the monkeys could be placed and would remain in various awkward positions. They continued to show interest in food and ate when aroused. In this profound state of inactivation the monkeys appeared to sleep or at times actually slept but they could be awakened at will.

Attempts to duplicate the action of Serpasil with either light anesthetic or subanesthetic doses of sodium pentobarbital or phenobarbital failed. Whenever drug effects could be observed after barbiturate medication they were combined with incoordination and ataxia. This was also true of repeated daily oral doses.

Effect on Electroencephalogram

The untreated, quiet, restrained monkey showed a characteristic electroencephalographic pattern with a basic rhythm ranging from 6 to 9 cps. and a voltage of 50 to 75 μv. (figure 3A1). When the animals were allowed to remain undisturbed in the darkened room, the record started to show trains of lower frequencies, spindle formation, and eventually "humps" of drowsiness (figure 3B2).

As described above, Serpasil in a range of 0.5 to 1 mg./kg. intravenously produced profound changes in the behavioral pattern of monkeys. The basic electroencephalographic pattern taken at one hour intervals for four hours after drug administration was essentially unchanged under these conditions (figure 3A2). An analysis of the frequency distribution after Serpasil in three animals averaged 7.7 ± 1.58 cps. as compared to 8.3 ± 1.73 cps. under control conditions (figure 5). This slight shift proved to be statistically significant ($0.02 < P < 0.05$). As in the monkeys under control conditions (figure 3B) patterns of drowsiness with spindling and humps were encountered if the animals were left undisturbed. However, any pattern of drowsiness could readily be eliminated by arousing the monkey.

In contrast to these findings, barbiturates given in effective intravenous doses did produce well known characteristic changes of the electroencephalographic pattern.[23] Under these circumstances the animals were unconscious, asleep, and unresponsive. The record showed a pattern typical of deep sleep in monkeys, namely basic rhythm of 1 to 2 cps. and a voltage of 100 microvolts and more (figure 3C). Arousal patterns could not be obtained.

Effect on Body Temperature

Rectal temperature was recorded hourly for seven hours and at 24 hours after drug administration. More than 35 separate experiments in which mon-

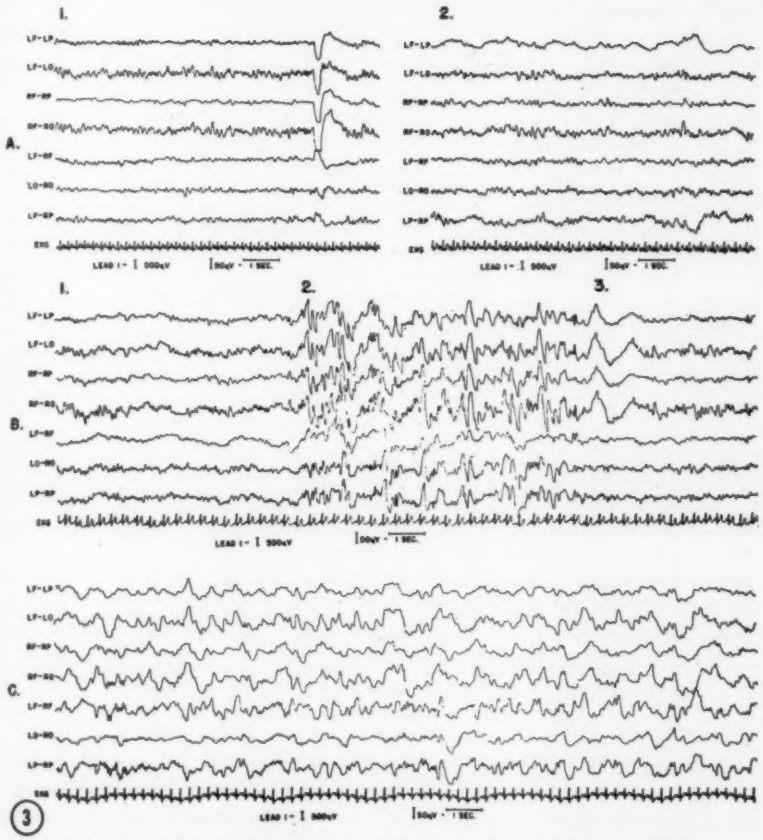

FIG. 3. Electroencephalograms of monkeys taken before and after administration of Serpasil and sodium pentobarbital, respectively. A1: Control record. A2: Record two hours after intravenous administration of 1 mg./kg. of Serpasil. Note the maintenance of alpha activity. B1: Normal control. B2: "Humps" of drowsiness as the monkey dozes off under control conditions. B3: Restoration of normal alpha activity after auditory stimulus. C: Monkey asleep after 23 mg./kg. of pentobarbital intravenously. Note the disappearance of alpha activity which is replaced by slow wave activity of one to two per second.

keys received single intravenous doses of 0.5 to 1 mg./kg. of Serpasil consistently showed a marked reduction in rectal temperature. At room temperature, which was kept constant at 74° F., the body temperature was regularly reduced from 4.5 to 5.5° F. within a five to seven hour period. The temperature gradually returned to normal control levels within 24 to 32 hours depending upon the dose (figure 4).

It was observed that the reduction of body temperature coincided with

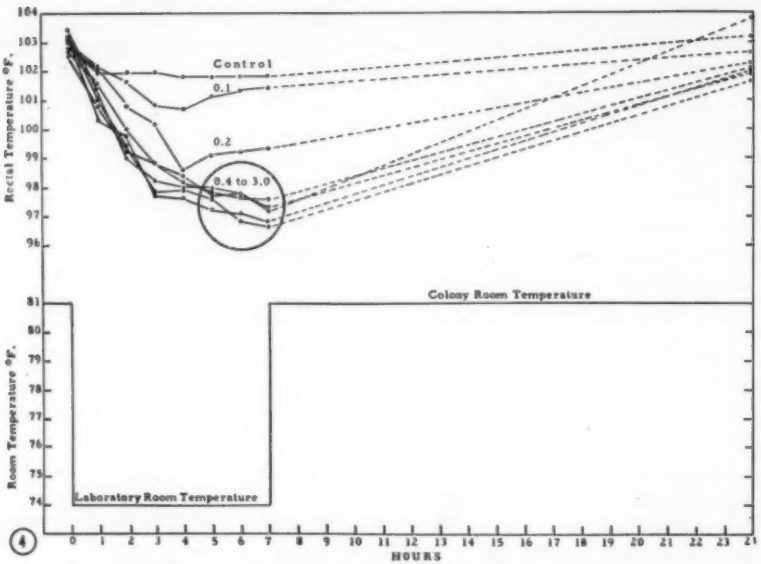

FIG. 4. Effect of graded intravenous doses of Serpasil on rectal temperatures in the monkey. Doses from 0.1 to 3.0 mg./kg. of Serpasil were given to three monkeys in eight different experiments, and the effect on body temperature was followed for seven consecutive hours and again recorded 24 hours after medication. A minimum recovery period of five days was allowed between experiments. Each dot represents the average of three determinations. Note that the reduction in body temperature could not be enhanced beyond a minimal level by increasing the dose of the drug. The maximum drop in temperature obtained after doses of 0.4 to 3.0 mg./kg. proved to be statistically significant ($P < 0.01$).

the degree of general effect of the drug on the monkey. Doses beyond 1 mg./kg. prolonged only the duration of lowering of body temperature. In a few experiments it was possible to reduce the body temperature as much as eight degrees, but this was not the rule. In one animal tested it was found that this reduction in body temperature could be prevented by keeping the animal in an environment of 85 to 90° F. In this experiment the body temperature was observed to have risen one degree at the end of one hour. Upon removal to an environment of 74° F., the body temperature was immediately reduced.

At room temperature Serpasil-treated monkeys shivered, and this response was exaggerated upon exposure to cold (25 to 70° F.).

Cardiovascular and Respiratory Effects

Systolic blood pressure, heart rate, and respiratory rate were recorded at one hour intervals after intravenous or oral administration of the drug in 12 experiments.

The systolic blood pressure fell slightly during some of the experiments;

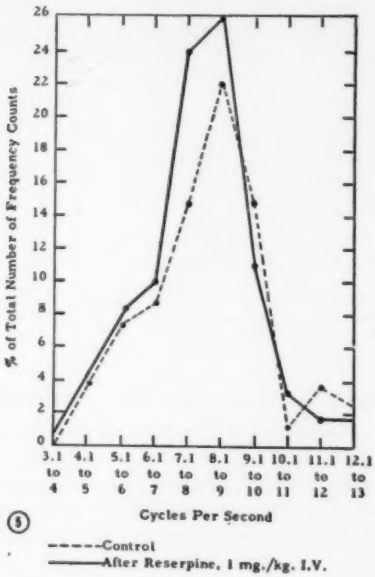

FIG. 5. Distribution of frequency in electroencephalograms of three Rhesus monkeys before and two hours after 1 mg./kg. of Serpasil intravenously. The average frequency of the controls was 8.3 cps. with a standard deviation of ± 1.73 cps., as compared to 7.7 cps. with a standard deviation of ± 1.58 cps. after Serpasil. This difference is statistically significant ($0.02 < P < 0.05$).

in others no change could be noted. In no case did systolic blood pressure reach values below 95 mm. Hg. No dose/effect ratio could be established.

The heart rate also dropped slightly in most experiments after administration of the drug, falling gradually over a period of hours.

The rate of respiration was unchanged or only slightly decreased over a period of hours. No change was noted in the type of respiration. Two typical experiments are presented in table 1.

Miscellaneous Effects

Miosis, a symptom which is common after administration of Serpasil in other species, was observed only to a very slight degree in the monkey. Pupillary accommodation to light was noted. Even after high doses maximal constriction of the pupil was not evident.

Flushing of the skin and nasal congestion were not observed, although an occasional animal showed signs of mouth breathing. Mild salivation was noticed in one animal.

At no time was there any change in the form of the stools. This was in contrast to other species, in which Serpasil may cause diarrhea.

No deaths have been encountered so far in doses up to 4 mg./kg. intravenously and 400 mg./kg. orally. Higher single doses have not been used because the volume of material presented problems of administration. The drug is remarkably nontoxic in the monkey as it is in other species.

TABLE 1

THE EFFECT OF SINGLE INTRAVENOUS DOSES OF SERPASIL ON SYSTOLIC BLOOD PRESSURE, HEART RATE, AND RESPIRATORY RATE IN ONE MONKEY

Criteria	*Dose mg./kg. i.v.*	*Control*	*Hours after medication with Serpasil*			
			1	*2*	*3*	*4*
Mean systolic blood pressure (mm. Hg)	1	154	150	138	132	116
	4	154	148	138	138	142
Heart rate per minute	1	240	230	210	220	240
	4	200	135	128	120	120
Respiratory rate per minute	1	34	34	30	32	34
	4	30	26	20	22	22

Note a slight decrease in systolic pressure which could be observed only in some of the animals. Decrease in heart rate and respiratory rate were observed regularly.

ACTION OF DAILY ORAL DOSES OF SERPASIL

Over a period of three months, three monkeys were given daily oral doses of Serpasil except during weekends. One untreated animal kept under the same conditions during that time served as a control. After a control period of about three weeks, the animals were started on very low daily oral doses which were progressively increased from 0.025 mg./kg. until an effect on behavior was noted at a range of 1 to 3 mg./kg. The animals were maintained at that dose. Body weight, body temperature, systolic blood pressure, heart rate, respiratory rate, and pupillary diameter were recorded at regular intervals. The tests were always performed following four to five days of consecutive daily medication.

In doses up to 1.0 mg./kg. no effect on the behavior of the animals was noted. Daily oral doses of 2 to 3 mg./kg. given for three to five days in the morning produced the same effects on behavior as single intravenous doses of 0.5 to 1.0 mg./kg. of Serpasil. One-half to one hour after administration of the drug the symptoms appeared. These effects gradually subsided toward evening. Miosis was not observed at any time and the body temperature was only slightly reduced for a short time after the oral dose of Serpasil.

As the systolic blood pressure readings, which showed a wide variation, were not significantly altered by Serpasil, the heart rate and respiratory rate showed a significant decrease. The body weight was maintained and the slight increase seen after three months was not statistically significant. These results are summarized in table 2.

DISCUSSION

Without doubt the most pronounced action of Serpasil observed in unanesthetized monkeys was the tranquilizing or inactivating effect. The term sedation is purposely avoided because it is usually employed for a different type of effect; the terms tranquilization or inactivation are chosen to indicate that a different site of action is involved in the Serpasil effect as compared

TABLE 2

EFFECT OF DAILY ORAL DOSES OF SERPASIL (2-3 MG./KG.) ON SYSTOLIC BLOOD PRESSURE, HEART RATE, RESPIRATORY RATE, AND BODY WEIGHT IN THREE MONKEYS

	Average control value	*Standard Error* $\sqrt{\frac{\sum d^2}{n(n-1)}}$	*Average value after chronic oral administration of Serpasil*	*Standard error* $\sqrt{\frac{\sum d^2}{n(n-1)}}$	*P value*	*Comments*
Mean systolic blood pressure (mm. Hg)	163	± 4.72	168	± 10.6	$> .5$	No significant change
Heart rate per minute	233	± 6.5	189	± 20.8	$< .01$	Significant decrease
Respiratory rate per minute	42	± 1.8	28	± 4.1	$< .01$	Significant decrease
Body weight (kg.)	4.5	± 0.28	5.4	± 0.54	$> .05$	Body weight maintained. Increase not significant

to other commonly used sedatives. Thus the monkeys under the effect of Serpasil invariably assumed their usual resting position and never lost coordination of activity. They could be aroused at any time, and even after very high doses a state of anesthesia was never observed. This is in contrast to the effect of barbiturates, which caused a certain amount of ataxia and incoordination in monkeys under the influence of subanesthetic doses and at slightly higher doses induced sleep from which they could not be aroused.

The electroencephalographic findings presented in this paper clearly demonstrate the difference in the effect of barbiturates and that of Serpasil. As Serpasil altered the behavior pattern of the monkey, the normal alpha activity seen in untreated animals was maintained. The importance and specificity of the slight slowing of the electrical cortical activity is not yet clear.

The monkey electroencephalograms showed periods of slow activity and higher voltage, indicating drowsiness and normal sleep from which they could be readily aroused. This picture was comparable to that observed in the normal untreated monkey (figure 3B). The normal pattern demonstrated in this figure corresponds well with the findings of Eldred and Trowbridge.[23] No matter how high a dose of Serpasil was given, the monkeys never showed tracings similar to those after effective doses of barbiturates.

It is interesting to note in this connection that the action of Serpasil can be readily differentiated from the effect of other central nervous depressants.[22] Its action was compared to antagonistic effects of sedatives such as barbiturates and sodium bromide on different types of seizures. In contrast to the effect of these drugs, Serpasil did not prevent chemically induced seizures, whereas a definite antagonism was found against audiogenic seizures.

Another typical effect of Serpasil in monkeys is the lowering of rectal temperature. The same type of reaction has been found in unanesthetized dogs

and rabbits.[20] A reduction of body temperature could be obtained at a dose level which roughly corresponds to that necessary to produce behavior changes. Increase in dosage did not enhance the fall in body temperature nor did it increase the tranquilizing effect. However, a prolongation of the effects at higher doses could be noted.

The hypotensive activity of Serpasil described in anesthetized dogs,[19] in anesthetized cats and rabbits,[16] and in unanesthetized hypertensive rats[24] could not be consistently demonstrated in unanesthetized normotensive monkeys. However, slowing of the heart rate and decrease in respiratory rate were present. Miosis, a symptom which is very pronounced in cats, dogs, and rabbits after higher doses of Serpasil, was not observed in the monkey. This corresponds to observations in man, where miosis is uncommon.[25]

Bein[16] and Bein, Gross, Tripod, and Meier[20] concluded that Serpasil acts directly on central autonomic substrates, possibly in the hypothalamus. Hess[26] showed that stimulation of certain nuclei in the supraoptic area of the hypothalamus of the cat produced a peculiar state of quiescence or sleep, associated with miosis, lowering of body temperature, fall of blood pressure, bradycardia, increased intestinal activity, and slowing of respiration. Based on their experimental evidence, Bein and co-workers[20] concluded that rather than a stimulation of these parasympathetic centers Serpasil caused a depression of the corresponding central sympathetic functions. The reactions of the monkeys to Serpasil were quantitatively different in many respects from the reactions of dogs, cats, rabbits, and rats. Symptoms such as the characteristic tranquilization combined with the lowering of body temperature, however, are signs of a change in the central regulating mechanism of the autonomic nervous system which are located in the brainstem. This gives interesting clues regarding therapeutic application of this drug in man where the psychophysical correlations are certainly of prime importance in the development of organic syndromes and psychosomatic disturbances.

SUMMARY AND CONCLUSIONS

1. Reserpine (Serpasil) was given to a group of Macaca mulatta monkeys in varying doses and by different routes of administration. The effect on behavior, electroencephalograms, body temperature, systolic blood pressure, heart rate, respiratory rate, and pupillary diameter were studied.

2. Single intravenous doses of 0.5 to 1 mg./kg. and single oral doses of 50 mg./kg. produce a state of quietude and unresponsiveness to extraneous stimuli, characterized by an essentially normal electroencephalogram, which clearly distinguishes it from sleep induced by barbiturates.

3. Parallel to the changes in behavior a drop in body temperature, an equivocal drop of blood pressure and a reduction of heart rate and respiratory rate were observed, whereas miosis and diarrhea, commonly seen in other species after Serpasil, were not present.

4. The threshold dose for chronic daily oral administration in the monkeys was 2 to 3 mg./kg.

5. Increasing the dose by all routes of administration did not enhance the effects observed but tended to prolong them. Toxic manifestations were not encountered after Serpasil in doses up to 4 mg./kg. intravenously and 400 mg./kg. orally.

6. The results of this study are in agreement with the experimental findings in other species and in man and further support the theory that the main point of attack of this drug is probably in the brainstem.

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The Status of Neurology as a Specialty in Various Countries

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and H. Houston Merritt, M.D.

IT HAS BEEN STATED frequently that neurology as a specialty is on the decline. In the United States, however, this is contradicted by several facts: many professorships have been created during the last few years, more time is given to the training of medical students in neurology, and a National Institute of Neurological Diseases and Blindness was founded recently. In order to study present trends in the status of neurology as a specialty, an international survey has been made, based partly on personal information obtained during the authors' trips and partly on correspondence with neurologists in other countries. It was hoped that common developments and trends might be recognized to give a starting point for better solution to future problems.

An important but by no means decisive factor in the standing of a medical specialty is its representation in the universities. In the United States an ever increasing number of medical schools have independent full professorships for neurology. In England, where neurology has contributed so much to our present day knowledge, there is only one full professorship, but neurology is represented in most teaching hospitals for postgraduate training within the framework of medicine. Similarly, there is no full chair for neurology in Switzerland. In both of these countries neurology is independent from psychiatry and more closely connected with internal medicine. France has independent professorships for neurology only in Paris and a few other universities. In most places neurology and psychiatry have a common chair for "neuro-psychiatry," but neurology is represented in all French universities, including Algiers, and also in some larger French cities in those medical schools which are not connected with a university.

Surveying the representation of neurology in the universities of most countries, the picture is quite variable and often does not reflect the actual importance of neurology in each country. The situation not only varies within the same country, but also in neighboring countries which are often thought of as closely related in their scientific organization. Thus, in Portugal neurology

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is represented in all three universities, although only one of them has a full professorship. In Spain, however, neurology is not represented in any university but is covered by the professors of internal medicine who are opposed to a separation of neurology from internal medicine. In the Latin American countries neurology has not developed after the example of their motherlands but resembles more that of the United States. All the Scandinavian universities have a strong representation of neurology. In none of these countries are neurology and psychiatry combined.

In many places neurology had to gain its independence from internal medicine; in others such as Holland, it had its roots in psychiatry. In Germany, where neurology developed equally from internal medicine and psychiatry, the trend seems to be towards an increasing independence from both, although only few full professorships for neurology alone exist. In most German universities, however, neurology and psychiatry remain combined. There is no difference between Western and Eastern Germany, although in Soviet Russia neurology is generally separated from psychiatry, as it is in Czechoslovakia, Rumania, and Poland; the two specialties are combined in Hungary. The development of neurology in the young country of Israel is designed along American lines and provides for an independent professorship of neurology in the country's only university. Otherwise, neurology is mostly limited to out-patient departments.

Historically, the close ties between neurology and internal medicine are demonstrated in the first academic lecture on neurology by the physician Boerhaave in Leyden, Holland in 1738, and the establishment of Romberg's first propaedeutic clinic in Berlin. As recently as 1945 a report of a special committee on neurology of the Royal College of Physicians in London emphasized the fact that neurology remains an important part of general medicine, and that much of the most valuable neurologic material is to be found in general medical wards. Yet, the report fully realized that the subject of neurology is now so large as to "occupy the whole professional time and energy of anyone who wishes to be a master of the subject."

It appears that today neurology is more closely linked to psychiatry than to internal medicine. This certainly is the case as far as the actual practice of the two specialties is concerned. The relationship also remains quite close in the universities of many countries. To a large extent neurology has been combined with psychiatry under a single professorship in Austria, Germany, and Italy. In Germany some individual neurologists succeeded in establishing chairs of neurology, but this was usually based on the personal prominence of the founders of such chairs, for example Foerster in Breslau and Nonne in Hamburg. In universities where the same hospital serves neurology and psychiatry, the advantage of such a program is that all assistants are trained equally in both fields. The objection is that one subject will often receive preference above the other. In Italy, for example, neurology always had a stronger representation than psychiatry in the majority of university hospitals. Yet a point in favor of such combined programs may be seen in the fact that

an Italian Neuropsychiatric hospital with great neurologic tradition gave us the most widely used treatment in psychiatry, namely the electric shock therapy.

The enormous expansion of both neurology and psychiatry makes it increasingly difficult for one individual to master both areas of medicine and, therefore, the trend toward a separation seems inevitable. It should be hoped, however, that the ties to psychiatry will not be severed completely either in research or in practical clinical work. While many feel that neurology has suffered from the enormous growth of modern psychiatry, it is equally true that psychiatry is in danger of becoming too one-sided, forgetting that the brain is the frequent origin of neurologic as well as of psychiatric disorders. The previously mentioned report on neurology by the Royal College of Physicians in London also stressed the close relationship of neurology and psychiatry because "each is concerned with the function of the brain, although from a somewhat different angle." Another consideration is that many psychiatric patients will continue to seek the advice of neurologists who, therefore, should be trained also in psychiatry.

The volume of neurologic activities cannot be measured from the work in the universities alone. Municipal hospitals often have special neurologic facilities or neurologic beds within a medical ward. In England, in view of the relatively small number of neurologic cases in small cities, it has been customary for a neurologist to visit several hospitals in a particular region in a consultant's capacity, with his headquarters in one of the large centers.

Hospitals for chronically ill patients have played an important role in the history of neurology. Since many neurologic disorders run a chronic course, any hospital for chronic diseases would have many such cases. Therefore, it became not unusual for such hospitals to install special departments as, for instance, the Montefiore Hospital in New York. This development had its origin in Paris, where the famous chronic neurologic wards of the Salpetriere and the Hôpital Bicêtre are centers of neurologic training and research. Our present survey indicates that this trend has not continued. Some of such chronic neurologic departments in Europe have been discontinued and few new ones established. There is no evidence that the number of chronic neurologic cases has in any way diminished. It may be, however, that the interest in this clinical material was greater in the past when the era of classification in neurology secured the greatest interest in the follow-up of such chronic cases to the point of verification of the clinical diagnosis by autopsy and neurohistologic study. Present neurologic research follows different procedures, and this may explain the diminished interest in chronic neurologic hospitals.

Special neurologic centers were organized after the first World War for cases of postencephalitis in Germany and Italy, but most of these were discontinued. Hospitals limited to poliomyelitis seem to exist only in the United States, where this disease nowadays is rarely considered the domain of neurologists, and in France, where it continues to be the responsibility of the neurologist. It appears that the acute cases of poliomyelitis are more and more in the hands of pediatricians and the chronic cases in the hands of

orthopedists. It is our impression that neurologic consultations as well as research by neurologists are more customary abroad.

There are also special neurologic hospitals for brain and spinal cord injuries. Hospital wards for paraplegics were organized after World War II in the United States and also in England. Brain-injured patients are taken care of in specialized hospitals, particularly in Germany where this trend started after the first World War in connection with special research interests on the part of German neuropsychiatrists.

The problem of rehabilitation as a whole is coming more and more into the foreground, especially in the United States. Since the end of World War II, the United States Veterans Administration has been chiefly responsible for rehabilitation of neurologically handicapped veterans. The rehabilitation of civilian neurologic cases such as patients with hemiplegia, spinal cord disease, and so on, has paralleled the increasing interest in neurologically handicapped veterans. The idea of rehabilitation has gained tremendous impetus during the last few years, and the neurologist can play an important role in the rehabilitation team. Children with cerebral palsy present another important neurologic rehabilitation problem.

In this survey, the development of neurosurgery in relation to neurology emerged as the most debated issue everywhere. No uniform trends can be seen as far as the future relationship between the two disciplines is concerned. In the same country various solutions of this problem may run parallel, giving a contrasting picture. The United States and England are the two countries where neurosurgery seems to be most firmly established as an independent specialty. In many other countries neurosurgery is still done by general surgeons. Among European pioneers in neurosurgery, some were general surgeons like Fedor Krause and de Martel, some were neurologists like Clovis Vincent and Otfrid Foerster who, after a long career in neurology, decided to train in surgery. While present-day European neurosurgery is becoming increasingly independent from general surgery, its position in relation to neurology is less clear. Some professors of neurology have a special neurosurgical unit in their hospitals, thus having neurosurgery under their direction. An impressive example that neurosurgery under neurology can gain great prominence is seen in Moniz of Portugal, a neurologist who is responsible for such important neurosurgical innovations as psychosurgery and arteriography. In a personal communication, Lima voiced the opinion that there should be only one professor for neurology and neurosurgery, and this should be a neurosurgeon fully trained in neurology. In this way neurology would follow a development similar to that of ophthalmology and otorhinolaryngology, which took over their own operative procedures. The actual trend, however, is best demonstrated in the three steps described by Monrad-Krohn in his own clinic in Norway. The neurosurgeon was first attached to the neurologic university hospital, later obtained a more independent neurosurgical subsection still within the neurologic hospital, and finally established an entirely independent neurosurgical unit.

Training in neurology, both undergraduate and postgraduate, cannot be compared easily in the different countries. In some of the larger medical schools of the United States students are given neurology in all four years of their curriculum. Clinical clerkships in neurology, customary in the United States, also exist in England and the Scandinavian countries, but rarely in other parts of Europe. The formal lecture is the chief medium of teaching in European medical schools. In universities where neurology and psychiatry are combined, the amount of teaching allotted to neurology often depends on the preference given to either field by the professor who holds the chair of these two specialties. One semester for both specialties together is the usual custom, but additional neurologic lectures are given by the professor of internal medicine. There are also non-obligatory lectures on neurology available to those students especially interested in this subject. Wohlfahrt in Sweden expressed the opinion that the precise scientific thinking inherent in neurology should be of great value to any medical student, and that it would greatly help him in his approach to other fields of medicine, a point which seems important in emphasizing the need for more neurologic training in the curriculum of medical schools.

Postgraduate training, too, lacks uniformity in the various countries. In the United States five years of training and experience are required for admission to an examination by the specialty board. Schools of specialization for neurology and psychiatry exist in some Italian universities. Elsewhere in Europe an assistantship of several years on a neurologic service rather than a formal examination is the requirement for recognition as a neurologist. Additional training in psychiatry and in internal medicine is usually requested. It is an interesting trend that in Sweden one of the three years of neurology may be spent in neurosurgery. Specialists in countries without formal postgraduate training normally spend many more years in full-time hospital work than are actually required. The importance of particularly thorough training of the neurologic specialist is stressed in the aforementioned report of the Royal College of Physicians with the very important reason that, while the majority of psychiatrists will work as specialist practitioners rather than as consultants, the small specialty of neurology will require most neurologists to work as consultants.

In neurologic research the trend toward training in the basic sciences, especially biophysics and biochemistry, is quite obvious. Such research is going on in many centers throughout the world. In the United States research in neurology is sponsored nationally by the newly founded National Institute of Neurological Diseases and Blindness. The Medical Research Council in England similarly aids research by keeping a special unit for neurologic research at Queens Square Hospital, and by giving other research grants for neurology elsewhere in the country. The trend towards special neurologic research institutes can be seen from such newly developed centers as the National Hospital of Neuropsychiatry in Argentina and a similar institute in Brazil. The main interest seems to be research in neurophysiology. Neuro-

pathology appears to hold its own in most countries.

The opinion that neurology is losing ground has been expressed by so many neurologists that it seems appropriate to list some of the reasons given, and to make some recommendations for remedying this situation. If medical neurology is becoming subordinate to neurosurgery, this development is best counteracted by a closer integration of the two fields. Many feel that neurology loses, while psychiatry gains in importance. In some countries, a greater number of young physicians prefer psychiatry simply because of the greater financial possibilities in psychiatry, while others are discouraged by the smaller number of hospital positions in neurology. Some feel that the newer methods of active treatment in psychiatry appeal more to the young physician, who is not willing to accept the traditional therapeutic nihilism of many neurologists. Here some criticism sets in, and many feel that it is the neurologist's own fault if he loses patients with therapeutic problems to the orthopedist, the physical therapist, and the rehabilitation specialist. Another area where neurologists should show a greater interest are the borderline problems between neurology and psychiatry. While acute brain injury is the concern of the neurosurgeon, the long-term treatment of these patients is best undertaken by the neurologist, whose interest should not stop at the determination of focal symptoms but follow through to the readaptation of the patient. It should also be realized that the huge field of psychosurgery offers an enormous challenge to the neurologist. These operations were based on neurologic experiences, mostly developed by neurologists, and should give great impetus to a specialty whose primary concern is the function of the brain. The role of the neurologist in psychosomatic problems has been stressed by Katzenstein-Sutro in Switzerland, and recently by Halperin of Israel in an article on "Neurology at the Crossroads." He emphasized the fact that neurology and psychiatry are closely associated because they reflect the twofold psychosomatic function of the nervous system. The modern somatic treatments in psychiatry, all of which have their basis in neurologic thinking, suggest a more psychoneurologic orientation of neurology in training, practice, and research.

In conclusion, it can be stated that neurology is still a specialty with many unfulfilled tasks, but its goals are shifting. It is moving beyond the nosologic work of the generation of the founders of neurology. From an organizational standpoint there is need for more neurologic centers equipped for clinical work as well as for research. Neuroanatomy and neurophysiology are likely to increase in their importance for human neurology, particularly if their clinical aspects are stressed. Neurology and neurosurgery should be well integrated. Interest should be developed in all borderline problems between neurology and psychiatry, orthopedics, and other specialties. Active consultation work by highly qualified neurologists must be given special attention and is the best way to convince representatives of other fields of medicine that there is continued need for a strongly represented neurologic specialty.

Studies on Experimental Concussion

Relation of Physiologic Effect to Time Duration of Intracranial Pressure Increase at Impact

E. S. Gurdjian, M.D., H. R. Lissner, J. E. Webster, M.D., F. R. Latimer, M.D. and B. F. Haddad, M.D.

IN PREVIOUS QUANTITATIVE DETERMINATIONS of intracranial pressure and acceleration at the time of impact, it was found that the time duration of the increase in the intracranial pressure was of importance in connection with the physiologic effects obtained.[1,2] In this paper the results of the effects of air pressure applied to the dural sac for varying time periods are given. By using an air piston it was possible to control the time duration of the pressure applied.

MATERIAL AND TECHNIC

Mongrel dogs were used in 72 experiments. The animals were anesthetized with Nembutal, using 1 cc. of 10 per cent solution per kilo of body weight. A trephine opening was made in the skull in the parietal region, and to it was attached the device with which it was possible to deliver a certain air pressure for a given duration of time.

The piston used for this purpose is shown diagramatically in figure 1. It may be noted that this is a cylinder containing a piston motivated by a spring. When the spring is released, the piston moves through the cylinder. First, air pressure of a given magnitude is permitted to come in contact with the dural sac, and as the piston moves further, the air pressure is permitted to escape at the same time that the flow of air pressure is stopped. By using this technic and changing the mass of the piston and size of the spring, varying speeds were obtained. A small, diaphragm type, strain gauge pressure pick-up was used to determine the pressure and its time duration, and photographic records were obtained from a dual beam oscilloscope. Pressure was supplied through an adjustable pressure-reducing valve from a tank of compressed air. Highest available air pressure was 120 pounds per square inch. Although 120 pounds per square inch was available in the tank, it was impossible to deliver this amount of pressure against the dural sac and transmit this pressure through the brain in very short time periods because of the size of the portal of entry through which the air passed and the volume

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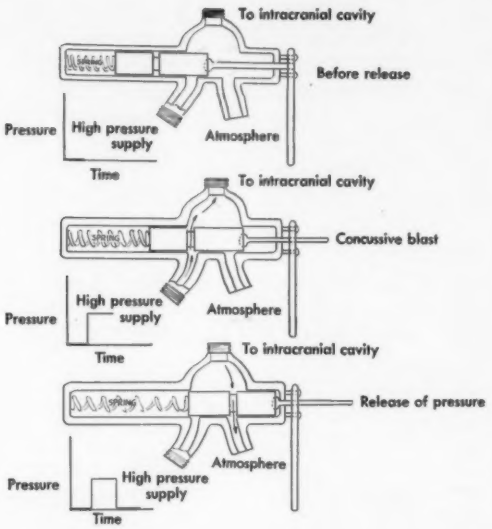

FIG. 1. Diagram of the device for producing time controlled pressures upon the dural sac.

which had to be filled. However, a definite trend of physiologic effects in proportion to the duration of the pressure was noted (table 1). It should be noted that records were obtained on the side of the brain opposite to that where the air pressure was applied. At the very high speeds, it is apparent that a pressure gradient will exist through the brain due to its inertia and the pressure measured by the pressure pick-up will be less than that applied to the side of the impact.

Another series of experiments reported upon in this paper include experiments on dog 27 through dog 48. A column of water was brought in contact with the dural sac through an opening previously made in the skull, into which was screwed a glass tube. By changing the weight of the cylindric iron bar and also changing the height from which it was dropped upon the column of water, different time periods of pressure and different levels of pressure were obtained. These records are summarized in table 2.

DATA

As may be seen in table 1, the results of the 72 experiments were classified on the basis of physiologic effects under conditions of no concussion, threshold concussion, moderate concussion, and severe concussion. Experimental concussion is characterized by a steep rise in blood pressure, with an apnea of the respiratory rhythm of varying duration. Under threshold concussion the pressure may not rise, in fact, in many instances it may fall and the respirations may not be completely arrested. In severe concussion the animals are

TABLE 1
"COMPRESSED AIR" CONCUSSION STUDIES
RELATION OF PHYSIOLOGICAL EFFECT TO DURATION OF PRESSURE

Dog Number	No Concussion		Threshold Concussion		Moderate Concussion		Severe Concussion	
	Pressure	Time	Pressure	Time	Pressure	Time	Pressure	Time
49					20	0.016		
50							20	0.046
51							20	0.044
52							36	0.014
53							29	0.006
54			20	0.045				
55			12	0.035				
56			13	0.037				
57			10	0.038				
58			13	0.020				
59	6	0.027	15	0.029				
60							30	0.030
61	15	0.002	18	0.002				
62	Dog dead at start of test.							
63			22	0.003				
64					25	0.003		
65	10	0.003	22	0.003				
66			17	0.003	27	0.003		
67			22	0.0022				
68			15	0.0018				
69					30	0.0017		
70	25	0.0011						
71			25	0.0015				
72	15	0.002	23	0.0018				
73	19	0.0019						
74			25	0.0018				
75							41	0.0012
76							35	0.0012
77					39	0.0012		
78					40	0.0016		
79					37	0.0012		
80					40	0.0011		
81	13	0.0010	22	0.0011				
82					40	0.0010		
83	No pressure record obtained.							
84			36	0.0011				
85	No pressure record obtained.							

mortally wounded even though they may survive the injury for several minutes. The pressure in pounds per square inch and its time duration are given. A pressure of 25 pounds per square inch may be unassociated with a concussive effect if its time duration is short enough, but the same amount of pressure lasting 1/50 second almost always causes severe concussion. Characteristic results are indicated in experiments 91 and 94 where 32 and 30 pounds per square inch, respectively, acted upon the dural membrane for 0.0014 and 0.0012 seconds, respectively, and failed to produce concussion (table 1). Yet in experiments 64 and 66, 25 and 27 pounds per square inch lasting 0.003 second resulted in a moderate concussion. In experiments 50 and 51 severe

TABLE 1—*(continued)*

Dog Number	No Concussion Pressure	No Concussion Time	Threshold Concussion Pressure	Threshold Concussion Time	Moderate Concussion Pressure	Moderate Concussion Time	Severe Concussion Pressure	Severe Concussion Time
86	26	0.0009						
87							32	0.0016
88			21	0.0023				
89			22	0.0013				
90			23	0.0010				
91	32	0.0014						
92	33	0.0018						
93							48	0.0014
94	30	0.0012						
95					35	0.0010		
96					27	0.0016		
97			33	0.0011				
98	6	0.004						
99			21	0.004				
100	31	0.0025						
101			22	0.0036				
102	4	0.0033						
103			5	0.0043				
104			10	0.00064				
105	No pressure record obtained.							
106							11	0.0024
107	12	0.0008						
108								
109	5	0.0012						
110	9	0.0012						
111	15	0.0027						
112	23	0.0023						
113	20	0.0011						
114	25	0.0027						
115	16	0.0012						
116	16	0.0025						
117							74	0.12
118	No pressure record obtained.							
119	No pressure record obtained.							
120					23	0.0068		
121							74	0.0031

Experiments with air pressure with varying time duration. Note that under moderate concussion, as the pressure increases, the time is shortened.

concussion was obtained with the application of 20 pounds per square inch lasting for approximately 1/25 second. With higher pressures the time duration for a severe effect was much less, as may be seen in the columns under severe and moderate concussions. Characteristic patterns are portrayed in figures 2 through 6.

In experiments where an iron cylinder was dropped on a column of water in contact with the dural membrane, essentially the same type of results are obtained. In experiments 38, 42, and 47, pressures of 21, 23, and 21 pounds per square inch lasting for 0.012, 0.0093, and 0.016 seconds, respectively, resulted in moderate concussive effect, while in experiment 45, pressure of 23

TABLE 2

STUDIES OF CONCUSSION CAUSED BY DROPPING WEIGHTS ON WATER COLUMN IN CONTACT WITH DURA

Dog Number	No Concussion		Threshold Concussion		Moderate Concussion		Severe Concussion	
	Pressure	Time	Pressure	Time	Pressure	Time	Pressure	Time
27							26	0.018
28							34	0.028
29			12	0.01				
30							49	0.004
31							44	0.013
32							50	0.013
33							48	0.014
34			20	0.013				
35			27	0.013				
36			24	0.019				
38					21	0.012		
39			28	0.012				
40	21	0.011						
42					23	0.0093		
44			28	0.015				
45							23	0.021
46	19	0.0076						
47					21	0.016		
48	22	0.013						

Note that the time factor is relatively constant. As the pressure is increased the physiologic effects become more severe.

pounds per square inch lasting for 0.021 seconds resulted in a severe concussion (table 2).

In experiments where both air under pressure was used and weights were dropped upon a column of water, the figures of pressure shown under severe concussion are not necessarily the minimum pressures required to achieve severe concussion.

In figure 7 the pressure in pounds per square inch in relation to the time in seconds has been recorded to show the relationship between pressure time and degree of cerebral concussion. It may be noted that the severe concussive effects fall in that portion mainly above the line C, while the threshold and moderate concussions are below the line C. It should also be noted that the longer the duration of the pressure exerted upon the brain, the lower the pressure required for a severe result. The shorter the duration, the higher is the pressure required to result in a severe effect. The fact that in this paper a certain number of severe concussive effects appear to fall below line C might be due to the condition of the animal resulting from unknown or the anesthesia factors. Nevertheless, a definite trend is suggested by figure 7, the material for which is obtained from table 1.

DISCUSSION

The findings discussed in the previous paragraphs appear to be significant. For concussive effects high pressures may be utilized for shorter periods

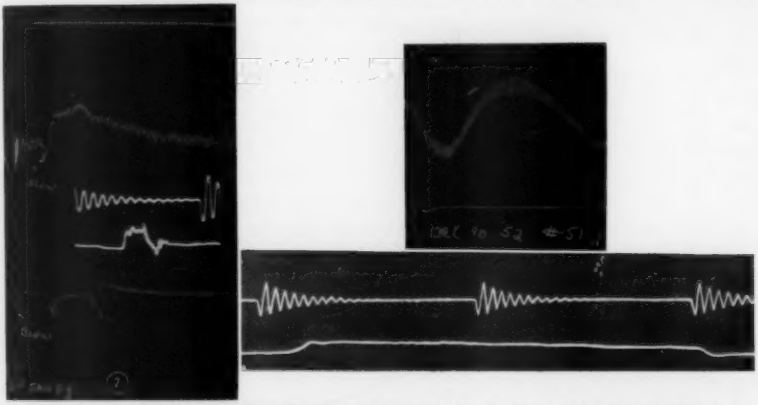

FIG. 2. Experiment 63 — Moderate concussive effect resulting from the application of 22 psi* for .0032 seconds. Oscillographic record placed on the kymographic record of time, blood pressure, and respirations. Oscillographic record of time and intracranial pressure, all from above downward.
FIG. 3. Experiment 51 — Fatal concussion resulting from the application of 20 psi for .044 seconds. Kymographic record of blood pressure and respirations. Below, oscillographic record of time and pressure.

*psi — 1 pound per square inch is equal to pressure of 30 mm. Hg pressure.

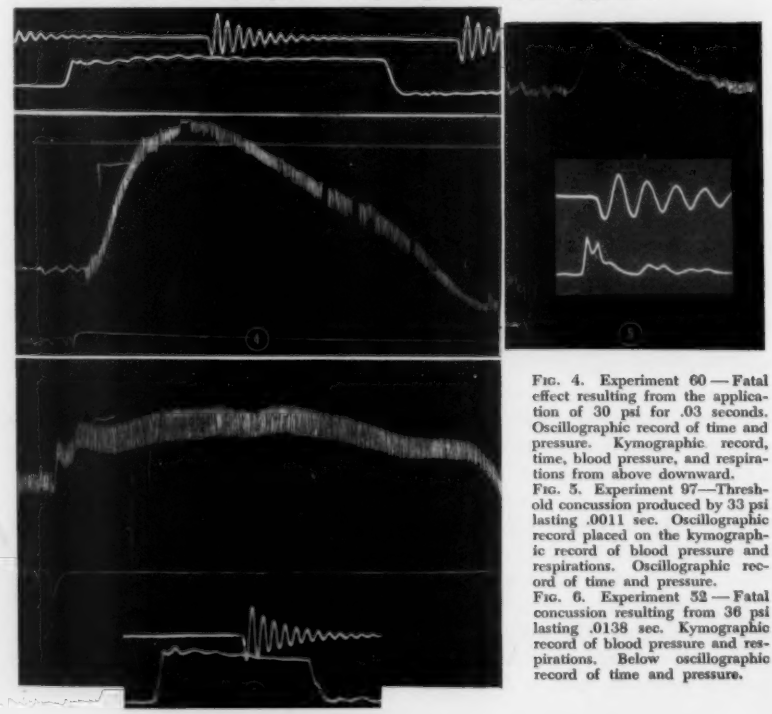

FIG. 4. Experiment 60 — Fatal effect resulting from the application of 30 psi for .03 seconds. Oscillographic record of time and pressure. Kymographic record, time, blood pressure, and respirations from above downward.
FIG. 5. Experiment 97—Threshold concussion produced by 33 psi lasting .0011 sec. Oscillographic record placed on the kymographic record of blood pressure and respirations. Oscillographic record of time and pressure.
FIG. 6. Experiment 52 — Fatal concussion resulting from 36 psi lasting .0138 sec. Kymographic record of blood pressure and respirations. Below oscillographic record of time and pressure.

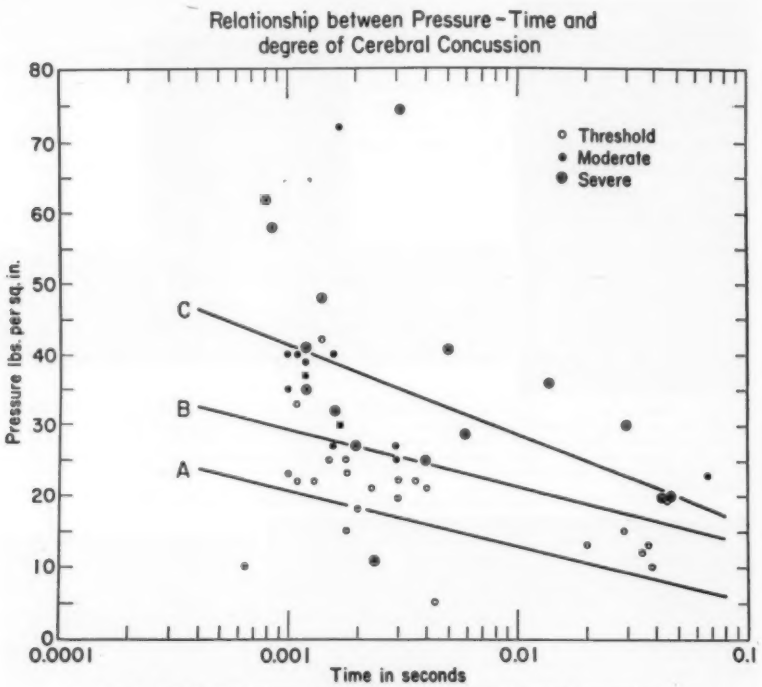

FIG. 7. Relationship between pressure, time, and degree of cerebral concussion.

of time than if lower pressures were used. Under the latter circumstance the lower pressures must act upon the brain for longer time periods in order to result in equal concussive effects. Since acceleration studies (using barium titanate and the Statham strain gauge type accelerometers) show no correlation between the degree of cerebral concussion and the level of the acceleration in G's, the conclusion may be drawn that acceleration results in rises in intracranial pressure causing a concussive effect depending upon the time duration of this rise. With an elevated intracranial pressure of a short duration the effect is minimal or absent, whereas if the acceleration resulted in a more prolonged rise in intracranial pressure, then a concussion was produced.

These findings also explain the occasional but well documented occurrence of perforation of the skull and brain by very fast moving small shell fragments unassociated with unconsciousness. The explanation for this occurrence is most probably the fact that the induced intracranial pressure is of such short duration that no concussive effect results.

In the mechanism of head injury with resultant concussive effects if the head is relatively fixed, a direct blow upon the head results in an increase in

intracranial pressure lasting for a longer period of time than if the head were free to move at impact with a similar blow. Under the latter circumstance, higher velocities with effective masses are needed in order to cause a concussion. When the head is free to move, the increased intracranial pressure is of shorter duration since the head moves with the completion of the impact as its inertia is overcome. With the head fixed, the impact tends to act for a longer period of time upon the cranium and its contents.

The above experimental data reinforce the conclusion that acceleration, deceleration, and compression result in measurable pressure elevations in the intracranial cavity. Under the circumstance of relatively pure acceleration, higher levels of pressure are necessary to obtain the concussive effect, since the duration of the increased intracranial pressure must be much shorter than if a compression or deceleration type of injury was the cause of the concussive effect.

A blow to the head produces increased intracranial pressure by two mechanisms: 1) by deforming the skull which results in relatively uniform pressure increases, and 2) by accelerating the skull which produces an increased intracranial pressure on the side of the blow, a pressure which is lower or decreases to zero or below on the opposite side.

It may be noted that at high pressures delivered for short time periods, it was impossible to record a square pressure wave on the side of the head opposite that to which the pressure was introduced, because of the inertia and natural frequency of the brain itself. Records in cases where high pressures were delivered for short time periods indicate one or more cycles of pressure and it was necessary to estimate an average pressure and time duration from the record. At lower pressures, good square pressure time waves were obtained.

CONCLUSIONS

1. An experimental study of head injury has been carried out, in which the time duration of the increased intracranial pressure at the time of impact is controlled.

2. The experiments show that the shorter the time duration the higher the pressure necessary to result in a concussive effect. The longer the time duration the lower can the pressure be in order to effect a concussion.

3. Concussion resulting from acceleration, deceleration, or compression is caused by an increase in intracranial pressure at the time of impact. With compression an increase in intracranial pressure is more uniform throughout. Acceleration or deceleration injuries result in increased intracranial pressure with pressure gradients in the cranial cavity.

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Treatment of Parkinsonism with Pagitane Hydrochloride

Results in 142 Patients

Adolfo Zier, M.D. and Lewis J. Doshay, M.D.

THAT new and better remedies are needed for Parkinson's disease has been amply documented.[1,2] Those who work with large numbers of patients with parkinsonism find it so, for the following reasons:

1. Although the armamentarium has been materially augmented by the addition of synthetic drugs, there is much that remains to be done. Major tremor, for example, continues to be a grave challenge to therapy. While hyoscine and Benadryl[3] control it in some patients, others are not controlled, with or without these remedies.

2. Drugs have a tendency to wear off in effect. Hence, sufficient high-grade preparations must be available to allow for substitution.

3. No single drug can control all the symptoms of an advanced patient. A product that inhibits tremor through its somnorific effect, by the same token aggravates the akinesia. Conversely, strong cerebral stimulants that counteract akinesia tend to accentuate the tremor. Thus, some patients require two, three, or even four different preparations at the same time, and a large selection of potent drugs is needed therefore.

4. During the long siege of an illness that runs ten or more years in the arteriosclerotic type of patient and 20 to 30 years in the postencephalitic type, patients tire of any remedy. As a result, many of them are forever seeking the newspapers, clinics, and doctors' offices for new drugs or so-called "cures."

5. Patients differ radically in their tolerance of drugs. While a postencephalitic type of patient may be satisfactorily adjusted on 45 tablets of Rabellon a day, an arteriosclerotic patient may not tolerate even ¼ of a tablet twice daily without complaints of violent reactions. Elderly patients are especially sensitive to drugs, and frequent substitutions are necessary. It often becomes a problem to find sufficient remedies to keep them satisfied and physically comfortable.

For these and other reasons, a great need exists for useful remedies that

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will meet the ever-changing tastes, tolerance, and reactions of patients with parkinsonism. The present paper deals with experiences with one such new product, Pagitane hydrochloride.[4,5,6]

CHEMISTRY AND PHARMACOLOGY

Pagitane hydrochloride, 1-phenyl-1-cyclopentyl-3-piperidino-1-propanol hydrochloride, is a new synthetic that is closely related in structure to trihexyphenidyl (Artane), which bears the chemical formula 3-(1-piperidyl)-1-phenyl-1-cyclohexyl-1-propanol hydrochloride. Pharmacologic studies of Pagitane hydrochloride have shown its antispasmodic properties to be half as effective as atropine. On the other hand, it has only a tenth of the inhibitory action of atropine on the cardiac vagus and about a tenth of its antisialogogue potency. Animal toxicity studies revealed no evidence of damage to the organs or blood constituents. Thus, Pagitane appears to possess large elements of the favorable effects of atropine and far less of its disturbing components.

MATERIAL AND PROCEDURE

Pagitane hydrochloride was originally supplied for investigation in the form of 2.5 and 5 mg. scored white tablets. This made possible the administration of 1.25, 2.5 and 5 mg. doses. The drug is now available on prescription in pink 1.25 mg. and red 2.5 mg. tablets.

The present study was begun in the fall of 1952 with a small series of cases which has since expanded to include over 200 patients, although only 142 which have been observed most closely and for the longest period of time are reported here. These 142 patients were a selected group in the sense that they had failed to respond to other anti-Parkinson drugs. Eighty-five were men and 57 women. Their ages ranged from 37 to 77 years. They were scattered among the three types of parkinsonism in the following ratios: 45 (32 per cent) were postencephalitic, 50 (35 per cent) were idiopathic, and 47 (33 per cent) arteriosclerotic. The duration of treatment ranged from days to 15 months. However, patients were not evaluated as improved unless they had remained under treatment at least eight weeks.

It was found that younger patients readily tolerate a starting dose of 2.5 mg. three times a day and older patients 1.25 mg. twice daily. The usual procedure is to slowly increase the dose by adding either a full or half tablet each week until optimal dosage is reached. The optimal maintenance dose ranged from 2.5 to 5 mg. three to five times a day among young patients and from 1.25 to 2.5 mg. two or three times a day among older patients. Postencephalitic patients, who generally suffer from high degrees of sialorrhea, were advised to take the medication before meals and elderly patients, after meals.

RESULTS

Admittedly, emotional factors are known to materially affect the results of treatment.[7] However, since machines have not yet been devised that can

provide precise information as to the effects of a drug, estimations of Pagitane had to rest on the clinical observation of changes in the patient, on frequent rechecks, and especially upon reports from the patient and his family. Provided that a large enough series of cases is employed to neutralize errors and that the sampling is sufficiently distributed among the three types of parkinsonism, a trained observer can arrive at fairly accurate evaluations by such a procedure, even in the absence of precise measuring instruments. Improvised tests, such as the speed of walking 100 feet, transferring marbles or coins from one box to another, striking a key with a finger, and the use of placebos are too strongly steeped in emotional factors to be of conclusive value, even though they may serve as handy supplementary procedures. Electromyography, which is fairly specific as a diagnostic tool in parkinsonism, is of limited if any value as a procedure for measuring changes produced by drugs.[8] The basic criteria employed in this study as an index of improvement were a decrease in rigidity, reduced severity of tremor, increased ability to perform daily activities, and favorable changes in speech, writing, spirit, and general behavior.

TABLE 1
RESULTS OF TREATMENT WITH PAGITANE HYDROCHLORIDE

	Idiopathic 50 cases (35%)		*Arterio-sclerotic 47 cases (33%)*		*Post-encephalitic 45 cases (32%)*			
	Number	*Per cent*	*Number*	*Per cent*	*Number*	*Per cent*	*Total*	*Per cent*
Improved	29	58	31	66	34	75	94	66
Unimproved	17	34	15	32	8	18	40	28
Worse	4	8	1	2	3	7	8	6
						Total	142	100

Ninety-four (66 per cent) of the 142 patients showed improvement of varying degree, while 40 (28 per cent) were unimproved and eight (6 per cent) became worse (table 1). Seventy-six patients (53 per cent) claimed a reduction in the stiffness of the muscles; 51 patients (36 per cent) stated that the severity of the tremor was decreased; and there was an increase in the feeling of well being in 38 patients (27 per cent). Eight patients or 6 per cent of the series claimed that they felt more relaxed (table 2). Magee and DeJong[1] found 46 per cent of their cases improved. Such moderate differences in results between investigators are understandable, considering that we possess no precise tools for measuring changes and the clinical criteria for improvement differ to some extent.

Nine patients out of a total of 18 with oculogyric crises experienced either complete control or a lessening in the frequency and severity of attacks. In some cases the attacks were regularly aborted by 5 or 10 mg. of Pagitane taken just before the onset, which the patients generally recognized by a tightening in the ocular muscles.

TABLE 2
DETAILS OF FAVORABLE RESPONSES WITH PAGITANE HYDROCHLORIDE*

	Idiopathic (50 cases)	*Arteriosclerotic (47 cases)*	*Postencephalitic (45 cases)*	*Total (142 cases)*
Rigidity improved	26	29	21	76 (53%)
Akinesia improved	25	10	21	56 (40%)
Tremor improved	22	13	16	51 (36%)
General feeling of well being	12	7	19	38 (27%)
More relaxed	4	2	2	8 (6%)
Stronger	5	3	0	8 (6%)
Speech improved	2	0	4	6 (4%)
Oculogyric crises improved	0	0	9	9 (50%)†

*Most patients showed improvement in more than one of the items.
†Nine out of 18 patients with oculogyric crises showed either complete control of or reduction in the number and severity of the attacks.

As with Artane, some patients had to employ hyoscine or Benadryl along with Pagitane for the control of severe forms of tremor, and atropine or Cogentin (MK-02)* for the control of advanced states of rigidity. Of the total number of patients, 40 (28 per cent) received Pagitane hydrochloride as the sole therapeutic agent, while the remaining 102 (72 per cent) required the simultaneous use of one or more of the preparations listed in table 3. It might seem from this that few patients used Pagitane alone. This was not actually so, however, since table 3 includes supplementary drugs even if used for only

TABLE 3
OTHER DRUGS GIVEN IN CONJUNCTION WITH PAGITANE HYDROCHLORIDE*

	Idiopathic (50 cases)	*Arteriosclerotic (47 cases)*	*Postencephalitic (45 cases)*	*Total (142 cases)*
Cogentin (MK-02)	21	28	16	65
Dexedrine	10	3	4	17
Benadryl	8	6	1	15
Hyoscine	2	6	5	13
Artane	4	2	4	10
Thephorin	4	4	1	9
Bellabulgara	1	0	3	4
Tolserol	0	0	1	1
Tr. stramonium	0	1	0	1
Rabellon	1	0	0	1
No other medication	16	9	15	40

*A number of patients had more than one additional drug.

*Cogentin (MK-02) is a product of Merck and Company. It has just been approved (March 1954) by the Food and Drug Administration and is expected to be released shortly.

a day. In most instances it was found that, month after month, the basic or only drug employed was Pagitane hydrochloride.

Early impressions were that the effects of Pagitane had a tendency to wear off quickly. Further observation, however, proved that a large percentage of cases had remained steadfastly on Pagitane for over a year and that many of those who switched back to their original treatment soon returned to Pagitane and have continued to derive satisfactory results. In only 20 per cent of the improved cases was it felt that the beneficial effects of Pagitane were diminishing after three to six months of use.

In addition to the cases of parkinsonism, two cases of familial tremor were treated with Pagitane hydrochloride. The dose was increased until the side reactions of blurred vision and dryness of the mouth were too disturbing to be tolerated. No improvement whatsoever was noted. A case of Huntington's chorea showed a pronounced reduction in involuntary movements on 2.5 mg. three times a day. The improvement has continued for 12 months. A 14 year old boy with dystonia musculorum deformans has been using Pagitane for the past 15 months. He feels greater strength and is less spastic. A case of pseudosclerosis failed to show any improvement on Pagitane.

On the basis of experience in 142 cases, Pagitane hydrochloride was found to be highly effective among patients in whom Artane treatment was losing its effects. It was also found that Pagitane can be employed as the basic drug for the control of all the symptoms of parkinsonism, except that other drugs may be required additionally to counteract either major tremor or advanced rigidity. Pagitane exerts an action against oculogyria, rigidity, sialorrhea, and mild forms of tremor, and it is highly effective as a cerebral stimulant. Brief case histories will illustrate the effects and range of dosage of Pagitane:

Case 1.—A 45 year old postencephalitic nurse suffers from oculogyric crises. She has gained greater relief from 2.5 mg. of Pagitane four times a day during the past ten months than on former remedies.

Case 2.—A 45 years old postencephalitic patient had not reported for eight months. She returned to state that 2.5 mg. of Pagitane fully aborted her oculogyria attacks within 15 minutes, where before they lasted all day. She finds Pagitane much better for the purpose than hyoscine, Benzedrine, Artane, or Vinobel.

Case 3.—A postencephalitic woman of 47 has been responding remarkably well to 2.5 mg. Pagitane three times a day for the past eight months. She has less drying effects than with Artane, which she had to employ in huge amounts. Her staring attacks have disappeared.

Case 4.—A 38 year old postencephalitic woman uses 10 mg. of Pagitane in addition to 10 mg. of MK-02 three times a day. She obtains great relief for the rigidity and tremor of one arm.

Case 5.—A 49 year old postencephalitic male could not tolerate hyoscine or Artane because of dryness. Pagitane in 1.25 mg. doses four times a day has controlled his tremor and rigidity for the past nine months, with minimal side effects.

Case 6.—A 42 year old postencephalitic has used 2.5 mg. of Pagitane three times a day for the past ten months, and his speech and gait are better than on previous medications.

Case 7.—A 39 year old postencephalitic patient was rigid, lethargic, and akinetic. Treatment with 5 mg. of Pagitane four times a day has kept him energetic and free in motion for the past 14 months.

Case 8.—A 57 year old patient with idiopathic parkinsonism finds adequate relief in 1.25 mg. of Pagitane twice daily for his tremor and rigidity.

Case 9.—A 66 year old male with idiopathic parkinsonism has done well for the past 14 months on 5 mg. of Pagitane four times a day, in addition to 2 mg. of MK-02 twice daily. Tremor and akinesia are under control.

Case 10.—A 65 year old idiopathic patient has used Pagitane, 2.5 mg. four times a day for the past four months, and feels less tired after a day's work than on much larger doses of Artane.

Case 11.—A 46 year old idiopathic patient obtains greater satisfaction with 2.5 mg. of Pagitane twice daily, than with Rabellon, stramonium, and Dexedrine in the control of tremor and akinesia.

Case 12.—A 55 year old tabetic with idiopathic parkinsonism has used 5 mg. of Pagitane three times a day for the past 15 months. He feels better and stronger than on Bellabulgara, Dexedrine, and Artane.

Case 13.—A 46 year old idiopathic patient was sensitive to Artane treatment while in Australia. She arrived in this country to seek help and adjusted satisfactorily to 2.5 mg. Pagitane three times a day. She returned to Australia six months ago and writes that her tremor is less, that she feels freer in body, and was able to dance for the first time in two years.

Case 14.—A 69 year old arteriosclerotic patient has used 2.5 mg. Pagitane twice daily for 15 months and finds greater relief from tremor and rigidity than on hyoscine and Bellabulgara.

Case 15.—A 69 year old arteriosclerotic patient obtained no relief for tremor when on Benadryl and Thephorin. He has been using Pagitane, 2.5 mg. three times a day, for 12 months with satisfactory results.

Case 16.—A 65 year old arteriosclerotic patient with advanced contractures in trunk and limbs finds it possible to travel to the clinic alone while on 5 mg. of Pagitane three times a day. He experiences much less dryness and mental confusion than when he used Artane.

Case 17.—A 57 year old arteriosclerotic parkinsonian patient has been on 2.5 mg. of Pagitane three times a day for the past five months. He finds it better than Artane and hyoscine for the control of tremor and rigidity.

Case 18.—A 64 year old arteriosclerotic patient has been taking 2.5 mg. of Pagitane four times a day for the past 16 months. He is greatly improved in strength and movement.

Case 19.—An arteriosclerotic woman of 65 has been on Pagitane for 14 months and likes it better than Artane because of minimal dryness and no mental clouding. She takes 5 mg. three times a day.

Case 20.—A 64 year old arteriosclerotic patient has been on 1.25 mg. of Pagitane three times a day for the past 12 months. Rigidity and posture are improved and he conducts his business with less fatigue than on former therapy.

SIDE REACTIONS

The side reactions were generally mild in degree and of similar nature to those produced by other belladonna agents and their congeners.[2] Those most commonly found were dryness of the mouth, 31 cases (22 per cent), and blurred vision, 18 cases (13 per cent) (table 4). Such events were never of serious proportions, even among arteriosclerotic patients who were on doses of 5 mg. Pagitane hydrochloride three times a day. A few patients, who had switched from Artane because its effect was wearing off but were anxious to try it once again, made much of one or the other complaint in order to gain their objective. By and large, however, most patients stated that Pagitane caused less dryness than Artane. A number of them acknowledged that they

TABLE 4
SIDE REACTIONS FROM PAGITANE HYDROCHLORIDE*

	Idiopathic (50 cases)	*Arteriosclerotic (47 cases)*	*Postencephalitic (45 cases)*	*Total (142 cases)*
Dryness of mouth	10	14	7	31 (22%)
Blurred vision	3	8	7	18 (13%)
Mental fogginess	2	5	2	9 (7%)
Weakness	4	1	3	8 (6%)
Restlessness	3	2	2	7 (5%)
Bladder retardation	1	1	2	4 (3%)
Constipation	1	1	1	3 (2%)
Headache	0	1	0	1 (1%)
Increased perspiration	1	0	0	1 (1%)

*A number of patients had more than one side reaction.

Pagitane hydrochloride (known in the experimental stage as Antispasmodic Compound 08958) is manufactured by Eli Lilly and Company. An expression of thanks is due the manufacturer for providing the necessary chemical and pharmacologic data and a liberal supply of the product.

had experienced unpleasant mental clouding when on Artane, but that they had not experienced such reaction with Pagitane.

No dangerous or disturbing side effects were noted among any of the patients under study. Minor reactions appeared among some patients during the early stage of treatment but disappeared later, and these were not included in table 4. Clinically, there was no evidence of blood dyscrasia, and routine checks of the blood were within normal limits.

SUMMARY

A new synthetic drug, Pagitane hydrochloride, has already been reported in the literature. The present report is a clinical survey of its action in a series of 142 patients with parkinsonism who had done poorly on other remedies. Of this number, 94 (66 per cent) manifested improvement of varying degree, 40 (28 per cent) were unimproved, and eight (6 per cent) appeared to be worse. The study covered a period of 15 months. Methods of administration and procedure are described.

Pagitane hydrochloride was found to be considerably more potent than Artane and less disturbing in its side reactions, especially dryness of the mouth and mental clouding. It is possible that within several years, as in the case of Artane, its effects may wear off in a larger percentage of patients than is evident now, or patients may tire of it and turn to some new preparation. Nevertheless, the fact that so many of them have chosen to remain on Pagitane for long periods of time and have continued to derive benefits from it establishes the drug as a valuable addition to the armamentarium for the treatment of parkinsonism.

Pagitane can be administered to all types of cases. Other than the usual side reactions of belladonna products and their congeners, it showed no toxic effects among any of the patients in this study. It is safe for both young and old patients, and may be employed as the drug of choice in starting treatment with new cases. It exerts a favorable action against rigidity, oculogyria, and mild forms of tremor. It is a powerful cerebral stimulant and serves to counteract akinesia, sluggishness, tiredness, and weakness. It readily combines with other drugs for more effective action against advanced stages of rigidity and tremor, such as hyoscine, Benadryl, atropine, MK-02, and so on. It is especially beneficial as a substitute for Artane among patients in whom the latter drug no longer controls symptoms.

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The coma into which the patient usually passes at the close of an epileptic fit often continues as heavy sleep, lasting for a quarter of an hour or longer, sometimes for hours. After the first few minutes, however, the patient can be roused. The sleep is usually followed by a severe headache, generally lasting for several hours more, and often continuing during the rest of the day. Both sleep and headache may be absent. Occasionally the sleep is not succeeded by headache, but if the patient is roused, and is not allowed to sleep, the pain in the head is severe.

W. R. Gowers in *Epilepsy and Other Chronic Convulsive Diseases*, published in 1885.

TREATMENT REVIEW

This section is designed to give prompt publication to the results of reliable studies in therapy, to record newer methods of treatment, and to encourage research in therapy of neurologic disorders.

AUGUSTUS S. ROSE, M.D., *Section Editor*

Recent Methods of Management of Spinal Cord and Cauda Equina Injuries

Comparative Study of World War II and Korean Experiences

Benjamin Boshes, M.D., Israel Zivin, M.D. and Eli L. Tigay, M.D.

INJURIES TO THE SPINAL CORD and cauda equina are common, but the sudden increase in numbers of these patients in war brings to focus the problems attendant to their care. Early mention came in the American Civil War[1] when 642 cases were reported (0.25 per cent). In World War II the incidence was 0.234 per cent. After World War I Frazier and Allen[2] described the general problem. The number of their cases was small because few lived to get home to America. Only 20 per cent were evacuated to this country, and of these 10 per cent survived the first year. Fewer than 1 per cent were alive in 1946.

Modern medicine has changed the hopeless, despairing attitude toward such cases. With the advent of the sulfonamides, the antibiotics, rapid transportation, and better rehabilitation methods, the entire philosophy of care for the spinal cord injured patient has been revolutionized. Reports during and following World War II documented what could be achieved with these patients if proper measures were instituted from the start. This required an appreciation of the pathology associated with the injury, both the changes in the spinal cord and emerging nerves, and a knowledge of the effects of the more remote changes, for example, in kidneys, bladder, and skin. The role of genitourinary infection, decubiti, and nutritional status had to be understood. The altered physiology of the spinal cord during the period of neural shock and of autonomous reflex activity had to be worked out. Autonomic nervous system dysregulation needed study.

From the department of neurology and psychiatry, Northwestern University Medical School, Chicago, and the division of neurology, Veterans Administration Hospital, Hines, Illinois.

TABLE 1
DISTRIBUTIONS — 100 RECENT CASES

	Battle Casualties		*Civilian Casualties*	
	PC	PI	PC	PI
Cervical	2	5	12	21
Dorsal	20	1	19	7
Lumbar	2	1	2	1
Cauda and conus	1	0	2	1
Cauda equina	0	3	0	0
Totals	25=71.4%	10=28.6%	35=53.8%	30=46.2%

PC=Physiologically complete
PI=Physiologically incomplete

Recovery of motion, sensation, and autonomic control was a new chapter in neurophysiology. Methods of rehabilitation, physical therapy, tidal drainage to restore reflex activity of the bladder, plastic surgery for correction of decubital defects, and procedures to restore adequate protein content of blood with correction of albumin-globulin relationships were gradually developed. To many investigators belong well-deserved recognition for pioneer efforts and persistence in the face of what appeared to be overwhelming odds. Only a few will be mentioned, because all cannot be listed. The reports of British neurologists like Head,[3] Holmes,[4] Riddoch,[5] and Walshe[6] and those of the German school, chiefly Foerster[7] and Marburg[8] are representative of the knowledge gained in World War I. Behind their studies stood the great contribution on neural integration of Sherrington in 1906.[9]

World War II added a tremendous impetus. The contributions of the American school, Munro[10] in Boston and at Cushing Veterans' Administration Hospital in Framingham, Massachusetts, Bors[11] at Birmingham Veterans Administration Hospital at VanNuys, California, Pollock[12] and his group at Hines Veterans' Administration Hospital, Hines, Illinois, and Davis[13] and Martin[14] in Chicago and at Hines, were numerous. Only summarizing references are mentioned; details may be found in their bibliographies.

The integrated program of research and rehabilitation initiated by the Armed Services and followed through by the Veterans' Administration after World War II is the basis of much of our present knowledge. From it has come a fund of information which has enabled the establishment of a comprehensive procedure for the care and rehabilitation of an individual suffering from an injury to the spinal cord or cauda equina.

Centers for the paraplegic veteran have continued to receive patients, chiefly fracture-dislocations from diving, automobile accidents, and falls, or the rare stabbing or gunshot occurring in civilian life. The Korean conflict changed this picture. Again the centers began to receive the war-wounded. The helicopter as a mode of rapid evacuation from the scene of injury and the more extensive use of the airplane shortened the interval between time of injury and that of possible definitive care. A fresh opportunity therefore has presented itself to examine the management of these patients, first to see if the lessons learned after World War II are being applied, and second to determine if the principles are valid.

THE ROLE OF LEVEL OF LESION

One hundred recent admissions to the Service for Injuries to the Spinal Cord and Cauda Equina at the Veterans Administration Hospital at Hines, Illinois

TABLE 2
100 RECENT CASES

Combined Battle and Civilian Casualties		
	PC	PI
Cervical	14	26
Dorsal	39	8
Lumbar	4	2
Cauda and conus	3	1
Cauda equina	0	3
Totals	60=60%	40=40%

were studied. These include 35 Korean War casualties and 65 civilian injuries (tables 1 and 2).

Tables 3 and 4 show fundamental difference between war and civilian cases. In the former group, 30 of 35 (85.7 per cent) were gunshot wounds. Of the latter, six of 65 (9.2 per cent) were by missile. Fracture dislocation made up 90.8 per cent. Of interest is the fact that 25 (71.4 per cent) of the battle casualties were complete, as were 20 of 21 dorsal lesions (95.2 per cent).

Table 5 shows a comparison of the recent and World War II material. The percentage of recent cervical cases is over four and a half times as great as the older series. This reflects earlier definitive care as will be discussed later. Dorsal lesions were about the same, while lumbar, conus, and cauda lesions were proportionately fewer.

A comparative analysis of the recent gunshot lesions, table 6, again shows that almost eight and a half times as many with cervical lesions survived for definitive care as in World War II. Dorsal cord lesions are slightly higher in the recent missile wounds, the rest proportionately lower. Again this reflects definitive care early.

EARLY CARE

Table 7 shows the known factors in evacuation of the recent cases. Battle casualties were usually littered to jeeps or ambulances and transported to the

TABLE 3
TYPE OF INJURY — 35 BATTLE CASUALTIES

	Physiologically Complete		*Physiologically Incomplete*	
	G.S.W.	*F.D.*	*G.S.W.*	*F.D.*
	25 cases=71.4%		10 cases=28.6%	
Cervical	1	1	5	
Dorsal	17	3	1	
Lumbar	1	1		
Cauda and conus	1	0	0	
Cauda equina	0	0	3	
Totals	20	5	10	
	G.S.W.—30		F.D.—5	

TABLE 4
TYPE OF INJURY — 65 CIVILIAN CASUALTIES

	Physiologically Complete		*Physiologically Incomplete*	
	G.S.W.	*F.D.*	*G.S.W.*	*F.D.*
	35 cases=53.8%		30 cases=46.2%	
Cervical	2	10	0	21
Dorsal	2	17	1	6
Lumbar	0	2	1	0
Cauda and conus	0	2	0	1
Cauda equina	0	0	0	0
Totals	4	31	2	28
	G.S.W.—6		F.D.—59	

TABLE 5
COMPARISON OF RECENT AND WORLD WAR II CASES — TOTAL DISTRIBUTIONS

	Recent		World War II	
	No.	%	No.	%
Cervical	40	40	23	8.7
Dorsal	47	47	125	47.3
Lumbar	6	6	37	14.0
Cauda and conus	4	4	37	14.0
Cauda equina	3	3	42	16.0
Totals	100		264	

TABLE 6
COMPARISON OF DISTRIBUTION OF CASES WITH GUNSHOT WOUNDS

	Recent		World War II	
	No.	%	No.	%
Cervical	8	22.2	5	2.7
Dorsal	21	58.3	95	51.0
Lumbar	3	8.3	26	14.0
Cauda and conus	1	2.8	28	15.0
Cauda equina	3	8.3	32	17.2
Totals	36		186	

nearest medical field operation or helicopter landing strip. Then they were carried to the closest evacuation installation, air field, or MASH hospital. Plane evacuation to Japan for definitive care and air transport to a paraplegic center in the United States followed in order. Only emergency treatment for shock, pain, or concomitant injury was instituted prior to rear area, MASH general hospital, or installation in Japan. Terrain features were hazardous and jostling unavoidable. Thirty-one of 35 were transported in the supine position. No casts were applied. In the 55 known civilian cases, all had relatively smooth ambulance transfer. Five of the 35 battle casualties received morphine for concomitant injury or shock. Tongs were applied early only in the civilian cases, in about half of the cervical cases and in an occasional dorsal injury (table 8). Twenty-one of the 33 cervical injuries in the civilian group were subsequently found incomplete. This, of course, is the surviving portion of those injured.

LAMINECTOMY

Sixty-three of the 100 patients had a total of 70 laminectomies (table 9). All of the battle casualties had this procedure. Table 10 shows the time factor. Civilian patients were operated on earlier because of more readily accessible hospitals.

CASTS

Seven patients, one battle casualty and six civilians had casts applied for concomitant injuries like a limb fracture.

TABLE 7
100 RECENT CASES — MODE OF EVACUATION AND TERRAIN FACTORS

	POSITION				TRANSPORT				TERRAIN		CAST
	Supine	Prone	Litter	Hand	Jeep	Ambulance	Train	Air	Rough	Smooth	
Battle casualties	31	4	27	2	20	12	2	34	30	5	0
Civilian casualties						55	Nothing else known				

TABLE 8
USE OF CRUTCHFIELD TONGS

	Battle Cases	Civilian Cases	
		Complete lesions	Incomplete lesions
Cervical	0	7 of 12 cases	11 of 21 cases
Dorsal	0	2 of 19 cases	1 of 16 cases
Lumbar	0		
Cauda and conus	0		
Cauda equina	0		

TABLE 9
LAMINECTOMIES — INCIDENCE AND DISTRIBUTION

	Battle Casualties				*Civilian Casualties*			
	Complete		*Incomplete*		*Complete*		*Incomplete*	
	Number Cases	*Number Lam.*	*Number Cases*	*Number Lam.*	*Number Cases*	*Number Lam.*	*Number Cases*	*Number Lam.*
Cervical	2	2	5	6	12	3	21	6
Dorsal	20	22	1	1	19	12	7	6
Lumbar	2	2	1	1	2	1	1	0
Cauda and conus	1	2	0	0	2	2	1	1
Cauda equina	0	0	3	3	0	0	0	0
Totals	25	26	10	11	35	18	30	13

BLADDER CARE

Bladder care was instituted promptly and internal catheters were placed in 30 of the 35 battle casualties. In some,

TABLE 10
LAMINECTOMY — TIME OF OPERATION

	Battle casualties 35 cases		*Civilian casualties* 65 cases	
1st day	9	=40%	13	=61%
2nd day	5		4	
3rd day	2		0	
4th day	1		0	
Later	21=60%		11=39%	

where later concomitant factors necessitated, a suprapubic catheter was installed to facilitate transportation. The present genitourinary status is seen in table 11. Among the battle casualties only four of 35 are able to do without catheters and only two manage with no device at all. This is related to the fact that 71.4 per cent of the lesions were severe and complete. In contrast, 17 of 65 or 26.2 per cent of the civilian patients have been able to discard their catheters. Sixteen need no device at all. Only 53.8 per cent of this group have complete lesions.

BLADDER STATUS

In a group of 37 recent patients where complete studies were available, 27 (73 per cent) had developed automatic bladders and six (16.2 per cent) were autonomous, emptying often in small spurts. These bladders were well on their way to becoming automatic. Thirty-one of the group studied were cervical or dorsal lesions (84 per cent). The figures, however, do not tell the entire story. The 100 recent patients have required only 11 lithotripsies, one renal nephropexy, and only one transurethral resection. In contrast, among the 283 patients studied in 1947-1948 there were 71 lithotripsies, two nephrolithotomies, two nephrectomies, seven resections of the bladder neck, and numerous lesser

TABLE 11
METHOD OF DRAINING BLADDER

	Battle Casualties					*Civilian Casualties*				
	Supra-pubic	*Int. Cath.*	*Ext. Cath.*	*Tidal Drain.*	*None*	*Supra-pubic*	*Int. Cath.*	*Ext. Cath.*	*Tidal Drain.*	*None*
Cervical	2	5	–	–	–	6	14	1	4	8
Dorsal	9	10	1	1	–	3	14	–	3	6
Lumbar	–	2	–	–	1	–	1	–	–	2
Cauda and conus	–	1	–	–	–	–	3	–	–	–
Cauda equina	–	1	1	–	1	–	–	–	–	–
Totals	11	19	2	1	2	9	32	1	7	16

TABLE 12
BLADDER STATUS. RECENT CASES — 37 PATIENTS

	Automatic		*Autonomous*		*Paradoxical Incontinence*		*Flaccid*		*Normal*	
	PC	*PI*	*PC*	*PI*	*PC*	*PI*	*PC*	*PI*	*PC*	*PI*
Cervical	1	11	1	2						
Dorsal	8	4	1	1	2					
Lumbar	2							1		
Cauda and conus										
Cauda equina		1		1						1
Totals	11	16	2	4	2			1		1

procedures. The recent patients have far fewer genitourinary infections and stones than those of World War II.

SEXUAL FUNCTION

As seen in table 13, 60 per cent had erections but these were chiefly reflex. Only 9 per cent had any awareness, and only 1 per cent had effective function.

BOWEL STATUS

As seen in table 14, only 16 per cent had truly reflex bowels, but 69 per cent initiated the movement digitally. By bearing down and manipulating the abdominal wall they were able to empty the bowel. Only 2 per cent had normal bowel movements in the full sense and 5 per cent had spontaneous evacuations. However in contrast to World War II figures, only 8 per cent were dependent exclusively on enemas. Six of the eight patients had physiologically complete

TABLE 13
SEXUAL FUNCTION

	Erections		*Awareness*		*Effective Function*	
	PC	*PI*	*PC*	*PI*	*PC*	*PI*
Cervical	8 of 14 57.1%	23 of 26 90%	0 of 0	2 of 23		
Dorsal	21 of 39 54%	3 of 8 37.5%	1 of 21	1 of 3		
Lumbar	2 of 4 50%	0 of 2	2 of 2		1 of 2	
Cauda and conus	0 of 3	1 of 1 100%		1 of 1		
Cauda equina		2 of 3 67%		2 of 2		

Total number with erections: 60=60%
Total number with awareness: 9=9%
Total number with effective function: 1=1%

TABLE 14
METHOD OF BOWEL EVACUATION

		Reflex		*Digital*		*Enema*		*Normal*		*Spontaneous*	
	Cases	*PC*	*PI*	*PC*	*PI*	*PC*	*PI*	*PC*	*PI*	*PC*	*PI*
Cervical	40		7	11	14		2		1	3	2
Dorsal	47	3	4	30	4	6					
Lumbar	6			3	3						
Cauda and conus	4			3	1						
Cauda equina	3		2					1			
Totals	100	3	13	47	22	6	2	0	2	3	2

dorsal lesions; the other two had incomplete cervical lesions and interruptions. In 1946, 100 per cent of the patients used enemas as the essential means of managing the bowel. In 59 of the recent cases, a cleansing enema is given occasionally, but not as a routine measure.

PAIN

Pain is always a distressing problem. Table 15 indicates that 46 patients (46 per cent) had pain as compared with 39.2 per cent of the World War II patients. No chordotomies have been necessary. There are no patients on opiates and no patients take alcohol to relieve this pain. Many patients do not speak of the pain unless asked.

SPASMS

Spasms were present in 72 per cent of the recent cases (table 16). As anticipated, the higher the lesion, the greater the frequency of spasms. The general distribution followed the figures of World War II except that there were fewer cauda equina and conus cases in the recent material, hence the higher over-all frequency. The breakdown by sections of spinal cord indicates an actual lower figure in the higher levels. What is more important is that, up to the two year period, only one patient had had an anterior rhizotomy, performed before he came to Hines. His was a physiologically complete dorsal lesion. Two patients had had an obturator section before coming to Hines. One lesion was cervical, the other dorsal. Both were physiologically incomplete. These figures stand in contrast to 18 rhizotomies among the 589 World War II cases studied.

DECUBITUS ULCERS

Bed sores used to be accepted as an inevitable accompaniment of the paralyzed patient, particularly the one with

TABLE 15
PAIN

	Battle Cases			*Civilian Cases*			*Comparison*	
	Pain		*Total*	*Pain*		*Total*	*%*	*%*
	PC	*PI*	*%*	*PC*	*PI*	*%*	*Recent cases*	*World War II*
Cervical	0 of 2	1 of 5	14.3	5 of 12	7 of 21	36.4	32.5	20.0
Dorsal	11 of 20	1 of 1	57.1	9 of 9	1 of 7	38.5	59.5	32.1
Lumbar	2 of 2	1 of 1	100	0 of 2	1 of 1	33	66.7	39.8
Cauda and conus	1 of 1		100	2 of 2	1 of 1	100	100	100
Cauda equina		3 of 3	100				100	100

Pain — Recent patients — 46%
World War II patients — 39.2%

TABLE 16
SPASMS

	Recent Cases						*World War II*
	Battle Casualties		*Civilian Casualties*		*Totals*		
	Number	*%*	*Number*	*%*	*Number*	*%*	*%*
Cervical	7 of 7	100.0	31 of 33	94	38 of 40	95.0	100
Dorsal	14 of 21	66.7	19 of 26	73	33 of 47	70.2	85
Lumbar	0 of 3	0	1 of 3	33	1 of 6	16.7	31
Cauda and conus	0 of 1	0	0 of 3	0	0 of 4	0	30
Cauda equina	0 of 3	0			0 of 3	0	0

Recent cases — 72 of 100 patients with spasm — 72%
World War II cases — 167 of 229 patients with spasm — 73%

1 rhizotomy
2 obturator nerve sections

TABLE 17
DECUBITUS ULCERS

	Recent Cases				*World War II Cases*	
	Battle Casualties		*Civilian Casualties*			
	%	*Number per patient*	%	*Number per patient*	%	*Number per patient*
On admission	31	2.5	38.5	2.08	68.0	2.6
Now	20	2.0	29.2	2.52	40.0	1.8
New	5.5	1.0	21.5	1.8	6.0	1.6

TABLE 18
PLASTIC SURGERY

Recent Cases		*World War II Cases*, 1946-1947
100 patients		Before admission to Hines: 83 patients had 129 plastic repairs, 62% successful
Needing plastic repair	12	
Number of repairs	17	Since admission to Hines: 67 patients had 92 operations, 57% successful

sensory as well as motor loss. Little wonder it was that the early cases in World War II had large necrotizing ulcers, especially sacral, with attendant infection and protein loss. Table 17 shows the comparative picture. Here again the figures need description. There were fewer ulcers on admission and fewer patients have them now. The figure for "new" ulcers still is high, but this is actually a sign of health. The lesions are small malleolar, ischial, or similar contact ulcers of a patient who is up in a wheel chair, in braces, or on crutches. The huge undermined ulcers of World War II are essentially gone.

PLASTIC SURGERY

The true state of the decubitus ulcer is seen in the plastic surgery table, table 18. The need for massive transplants is gone, because the large defects no longer occur. The ulcers are better cared for, and the patient does not reach the stage of extensive necrosis. Operative procedures are quickly successful.

GENERAL HEALTH

World War I and II reports emphasized the decline in the patient's health, particularly his weight loss, hypoproteinemia, and severe secondary anemia. Table 19 shows the decline in problems of weight loss. Transfusions which were a common procedure in 1946 are now a rarity. In 1946, 12.4 per cent of the patients showed an albumin-globulin reversal. None of the recent cases have shown this phenomenon. The general state of health of the recent patients is excellent.

RECOVERY

Earlier studies[15] indicated that most patients destined to recover do so in the first three months, but occasionally recovery may set in after the second and rarely even in the fourth year. Therefore the final chapter has not been written on the recent patient material. However, 22 per cent have shown sensory and motor recovery and 12 per cent autonomic function return. Of interest is the fact that in two instances among the 60 patients who had shown what appeared to be physiologically complete lesions, some sensory and motor return has occurred. In one instance some autonomic function was regained. These figures are similar to those of World War II

TABLE 19
WEIGHT LOSS

	Range of loss in pounds	*Mean loss in pounds*
Recent cases	8 to 56	19
World War II cases	10 to 120	55.6

where sensory return was found in 21 per cent, motor return in 20 per cent.[12] Of the 26 incomplete lesions, 12 (46.2 per cent) showed sensory and motor recovery and seven (17.5 per cent) showed autonomic return. The role of laminectomy in recovery is raised. Table 22 gives an idea of the factors involved. The general figure for laminectomized cases, 19.6 per cent, is not essentially different from the 20 per cent over-all figure for the recent or World War II groups. However, the battle casualties, all injured by missiles, with 71.4 per cent apparently complete lesions pull the figure down. Only 11.4 per cent show recovery. The civilian lesions, comprising 90.8 per cent fracture dislocations, bring this figure up; 33.3 per cent operated on show recovery. This is significantly higher than the over-all figure of 20 per cent.

PHYSICAL MEDICINE AND REHABILITATION

The ultimate question after medical care is, "What can the patient do?" Of 100 patients only eight are confined to bed. The others use wheel chairs. Thirty-nine per cent drive cars, but only 16 per cent use crutches. These men become so adept with wheel chairs that it becomes a problem to get them up on crutches. While only 5 per cent are in formal educational programs, over 80 per cent attend the rehabilitation shops regularly.

GENERAL ADJUSTMENT

This important aspect of the care of the spinal cord injured patient is interesting. In the recent 100 patients there are no essential disciplinary problems, no severe alcoholics, and no narcotic addicts. There have been no suicidal attempts and no psychotic episodes. In general they are a well-adjusted, cooperative group.

DISCUSSION

What may be gleaned from these new data? Are these figures different from those of World War II? The Korean war material, with the 30 cases of gunshot wounds out of 35 patients in this group (85.7 per cent), might be expected to have the higher proportion of complete interruptions of the spinal cord. This is so, 71.4 per cent as compared to 53.8 per cent. A comparison of the recent cases with those of World War II (table 5) indicates that a much greater number of severe cervical injuries are reaching centers for definitive care. The recent material contained four and a half times as many cervical injuries as that of World War II. Dorsal lesions were about the same, but lumbar, conus, and cauda lesions were proportionately less. Gunshot cases showed a much higher percentage of survival with cervical injuries, 22.2 per cent as compared to 2.7 per cent in World War II (table 7). This is eight and a half times as many. More patients with dorsal lesions also survived.

Why the higher survival? Table 7 indicates the mode of evacuation. Among the 65 civilian cases, 55 were known to have been moved by ambulance. This means trained personnel for lifting and careful littering. The battle cases were also quickly evacuated by jeep, ambulance, helicopter, and airplane. They were in hospitals for definitive care within a short time and in a center for the spinal-injured within days. Plane transport is safe for such patients. The argu-

ment of transferring the patient in the prone position as against the supine is resolved in the consensus of experienced investigators,[13] "The most important principle in the emergency treatment of fracture dislocations of the spine is to do nothing which will increase the bony deformity." Thirty-one of 35 battle patients were transferred in the supine position. The terrain was rough. How many injuries were aggravated by the exigencies of evacuation in war and how many died is not known. Crutchfield tongs (table 8) were used in 21 of 58 civilian patients, in 18 of 33 (54.5 per cent) cervical lesion patients, and in three of 25 (12 per cent) dorsal lesion patients. Tongs were not used for any of the battle cases, all gunshot wounds, but everyone had a laminectomy (table 9). Forty per cent of all war casualties and 61 per cent of all civilian cases had a laminectomy within the first four days after injury (table 10). This permitted debridement of the wound, removal of loose bone fragments, decompression of the cord, and drainage of blood and other fluid accumulations. The relationship to recovery will be discussed below. No patients had a cast applied for the spinal injury, and only seven of the 100 had a cast for concomitant limb fractures.

The care of the bladder is dependent upon when the patient is seen after the injury and what complications exist. Ordinarily an internal catheter had been instituted promptly. In some, a suprapubic catheter had been installed to facilitate transport on wound handling. When a patient arrives at a paraplegic center like Hines and no complications exist, the catheter is removed to determine bladder status. If the residual in the bladder is less than 100 cc. after a reasonable time, the patient is maintained without a catheter. If the residual is over 100 cc., the catheter is again instituted. An internal catheter is also used when there is dilatation of the ureters or increase in blood non-protein nitrogen. Suprapubic catheters are used when there are complications like epididymitis, fistulae, urethral abscess, recurrent infections, or inadequate drainage from below. If repeated infections have produced a fixed, shrunken, fibrotic bladder, catheter drainage is often needed.

Ideally, if ureteral reflux is not present, tidal drainage should be instituted as early as possible. The best results have been obtained by this method. However, this requires highly trained personnel and constant supervision of the apparatus. Since trained personnel are difficult to recruit and poorly supervised tidal apparatus results in complications, many installations do not use as much tidal drainage as would be desirable. Some patients, also, do not like to be confined to bed, as is often necessary in the tidal procedures. They prefer to be up and about all day. These are all factors in success in bladder rehabilitation and explain the differences in figures from hospital to hospital.

Of the Korean period group, 20 per cent still are on suprapubic catheter drainage (table 11). However, most of the patients (51 per cent) are still on internal catheters, 8 per cent on tidal drainage, 3 per cent on external catheter, and 18 per cent on no device at all. The last figure will rise as the bladder training program progresses. The civilian cases, with only 53.8 per cent complete lesions, show a higher bladder function recovery, 26.2 per cent, as compared to 8.6 per cent for battle casualties with 71.4 per cent complete lesions. Our experience with World War II cases would lead us to anticipate that more patients will discard all types of catheter drainage in the future.

The nature of the devices necessary for drainage reflects the physiologic state of the bladder: 62.2 per cent were de-

veloping automaticity; 46 per cent were fully automatic; 84 per cent of the patients had high lesions, cervical or dorsal, so that with proper care good reflex return could be anticipated. The improved genitourinary state is seen best in the fewer stones, rare lithotripsy, and in the now almost absent transurethral resection. Low incidence to absence of stones and infection means better functioning genitourinary systems and better general care.

Sexual function as summarized in table 13 still leaves much to be desired. Sixty per cent had erections, but this reflects the physiologic state of the spinal cord. Even among patients with complete lesions, 51.7 per cent had erections. Among patients with incomplete lesions, 72.5 per cent had erections, but none occurred among patients with complete cauda interruptions. Awareness was low, occurring in only 3 per cent of patients with complete and 12.5 per cent of those with incomplete lesions. The term "awareness" needs elaboration. It is difficult to conceive how a completely transected cord can transmit such feelings to central areas of perception. The spread of the sexual reaction through intact connections in the autonomic nervous system and the initiation of associated reflexes, somatic and visceral, may reactivate memories which the patient relates to the sexual feeling of his intact state. No true sensation of orgasm is felt in patients whose cord is completely transected above the sacral level. Only one patient (1 per cent) had effective function.

Paraplegic patients often marry, and sometimes the nurse is the bride. Coitus with intromission is possible under special physical arrangements with the female the aggressor. Fertility, however, depends on how much orchitis and epididymitis has preceded. The latter are still all too common.

The bowel status (table 14) reflects what has been said about the bladder. The training program is in progress and already 16 per cent of the recent cases have regained truly reflex function. Sixty-nine per cent initiated the movement digitally, and by developing technics in bearing down and manipulating the abdominal wall manually they are able to empty the rectum. Occasional cleansing enemas are used, but enemas as a means of bowel evacuation are necessary in only 8 per cent of the group, 6 per cent among those with complete and 2 per cent among those with incomplete lesions.

These figures stand in contrast to those of 1946 when all patients needed enemas. The price in personnel, linen, and patient's time, now much better employed, was high. When the bowel training was established at Hines, the findings were similar to those shown in table 14.[12] Enemas were needed in 8 per cent of that series. The remainder used digital extraction or reflex initiation. Only 18 per cent were truly automatic. As in the case of the bladder, with further training, bowel evacuation or reflex initiation rose to 63 per cent. It was the belief of the Hines group that, with further training, an 85 per cent goal would be reached.

Pain of the diffuse burning type, not root pain, was found often in our patients, 46 per cent as against 39.2 per cent in the World War II cases. Pollock's[12] idea of the pain was that it originates in the distal end of the proximal segment. Scarff and Pool[16] would attribute this to irritative foci, scars, spicules, foreign bodies, or hematomas at the site of injury. However, this diffuse discomfort tends to subside and often fades as a spontaneous complaint. In contrast to our World War II patients, nearly all of whom were taking narcotics when we received them, not a single recent patient has required an opiate. There are no patients taking alcohol to relieve pain.

No chordotomies have been necessary. There have been no absolute alcohol injections. In our World War II series 16 patients had 33 operations for chordotomy. Among these, five patients (six chordotomies) obtained no relief; in nine there was temporary relief. Sometimes the operation was followed by new and more severe pain than had existed previously. When the operation was done by an inexperienced neurosurgeon the danger of subsequent spasm or of a new more extensive lesion, higher in the cord, was increased. Our experience has been that pain diminishes to a low level in time and that surgery or other radical measures had best be postponed as a last resort measure.

Spasms are a common, troublesome complication (table 16). They interfere with the healing of decubiti, genitourinary infections, physical therapy and rehabilitation procedures, and may cause dislocation and fractures. Seventy-two per cent of our recent cases showed them. They are most common in cervical and high dorsal lesions, hence our high figure. However, only one rhizotomy and two obturator nerve sections, all done in the pre-Hines period, were necessary, as contrasted with 18 rhizotomies in our 589 World War II cases. Our experience with spasms would suggest that they usually reach a peak in the second year and then begin to subside. With fewer and smaller decubiti, fewer genitourinary infections, and better bladder and bowel control, the triggering mechanisms are reduced. In a control experiment studied elsewhere, a patient with a fracture dislocation at D7-8 had a unilateral rhizotomy to control the severe spasms. Both legs were implicated in the initial spasms. Surgery was done nine months post-injury. One year later, the spasms of the nonoperated side have subsided and give no trouble. Twenty-two per cent of our patients show motor recovery. It would be a pity to do a rhizotomy early to control spasms when some recovery may still set in. Therefore, we pursue a conservative course avoiding surgery unless it is absolutely necessary. Thus far not a single such need has arisen in our 100 cases. It may be added parenthetically that mass reflexes are very infrequent. As time after injury progresses, flexion postures usually associated with cervical or high thoracic lesions change to extension. The old concept that paraplegia in flexion or in extension is related to the completeness or severity of the lesion no longer obtains, as these patients survive into the stabilized period of chronic spinal man.

Decubitus ulcers are less frequent (table 17). Fewer than half as many recent patients had them on admission to Hines, 31 per cent as against 68 per cent in the World War II series. The number per patient and the frequency of new ulcers is about the same as for World War II. The difference lies in the type of decubitus. The huge necrotizing ulcers are no longer seen. Severe infections are rare. Plastic surgery (table 18) is infrequent in comparison to the old series. The new ulcers are small lesions at the malleoli, knee, ischium, all evidence that the patient is out of bed, in braces, wheel chair, or on crutches. The need for massive transplants in plastic repair is gone. It is noteworthy that casts in the early stages of wound care or transport are no longer used. Severe decubiti are not permitted to develop in easily inspected areas.

Fewer urinary infections and fewer and smaller decubiti result in improved general health. The mean weight loss (table 19) is much lower for the recent group, 19 pounds as compared to 55.6 pounds for the World War II series. Hypoproteinemia, albumin-globulin reversals, and severe secondary anemias are not seen and blood transfusions are a rarity (table 20). The recent patients look healthier and their vital data prove

TABLE 20
TRANSFUSIONS

	Recent Group—85 Cases 1951–1953	*World War II Group*—283 Cases 1946	1949
Transfusions	18	569	269

that this is true.

Our figures for motor, sensory, and autonomic recovery reflect those of the World War II patients (table 21). However, since some patients may still show return of function, these data are not yet final. Only 3.3 per cent of those which appeared to be physiologically complete lesions have experienced motor or sensory return, but those with incomplete lesions have shown 50 per cent recovery, and autonomic function has returned in 22.5 per cent. The role of laminectomy and Crutchfield tongs in recovery is raised. In the cervical group seven of seven battle casualties and nine of 33 civilian cases were operated upon; in 18 of 33 civilian injuries tongs were used. As noted above, four and a half times as many patients with general cervical lesions and eight and a half times as many with cervical gunshot lesions have survived, as compared to the World War II figures. Laminectomy and tongs are not the entire answer, but they may play a role. In the general laminectomized group the incidence of recovery was 19.6 per cent, not much different from the 20 per cent figure of the total recent or the World War II patients. Gunshot lesions with anatomical interruption of the lower cord anticipated benefits of surgery, 11.4 per cent with improvement, but the civilian dislocation does better, 33.3 per cent. The laminectomized patient is likely to be the more seriously injured, but as Covalt and associates[17] have shown, 3 per cent of the patients may improve even when the procedure is done at one year after injury. In the hands of the skilled neurosurgeon, laminectomy has little danger, does no harm, and gives the patient the satisfaction of knowing that everything possible has been done to help his injured spinal cord.

The factor of improved nutrition through control of infection and disturbed bodily function is also important in recovery. It is well known that a

TABLE 21
RECOVERY

		Sensory		*Motor*		*Autonomic*	
		PC	*PI*	*PC*	*PI*	*PC*	*PI*
Cervical	Cases	14	26	14	26	14	26
	Recovery	1	12	1	12	0	7
Dorsal	Cases	39	8	39	8	39	8
	Recovery	1	4	1	4	1	2
Lumbar	Cases	4	2	4	2	4	2
	Recovery	0	1	0	1	0	0
Cauda and conus	Cases	3	1	3	1	3	1
	Recovery	0	1	0	1	0	0
Cauda equina	Cases	0	3	0	3	0	3
	Recovery	0	2	0	2	0	2
	Cases	60	40	60	40	60	40
	Recovery	2=3.3%	20=50%	2=3.3%	20=50%	1=1.4%	11=27.5%
	Totals	22=22%		22=22%		12=12%	

TABLE 22
LAMINECTOMY AND RECOVERY

	Battle Casualties		Civilian Casualties	
	PC	PI	PC	PI
Number with laminectomy	24	11	19	12
Number with recovery	0=0%	4=36.3%	0=0%	7=58.3%
	4 of 35=11.4%		7 of 21=33.2%	
Totals	11 of 56 cases=19.6%			

severe urinary sepsis will wipe out motor, sensory, and reflex gains.

Physical medicine and rehabilitation continue to play a major role (table 23). Only 8 per cent of the recent group are confined to bed. The others are up and about in wheelchairs, on crutches, and driving cars. Being out of bed is an essential deterrent to stone formation and attendant genitourinary infections. While many ambulate in the physical therapy rooms up to one hour, they prefer their wheelchairs with which they become very proficient. It is a problem to get them to crutch-walk more frequently. Yet they handle the bladder and bowel functions well in this wheelchair existence, and they are careful about decubiti. Over 80 per cent are found regularly in the rehabilitation work shops, engaged in activities within the limits of their manual abilities, and 40 per cent of these are cervical lesion patients. The ambulation and other physical therapy programs continue with the same goal to make the patient as independent as possible. Five per cent of the patients are completing formal schooling.

Of greatest importance is the general adjustment of the 100 recent patients. There are no disciplinary problems, drug addicts, severe alcoholics, or disturbed patients. They fit into hospital routine and in general are a happy, well adjusted group.

CONCLUSIONS

1. A study of 100 recent patients, 35 battle casualties and 65 civilians, has been made and the results compared with a similar World War II period group.

2. The recent patients show a higher percentage of cervical lesions, a measure of better survival of the severely injured.

3. Better initial handling and rapid transport to centers for definitive care play a role in this improved state.

4. A program for bladder and bowel care is carried out to free the patient from dependence on bedside drainage or enemas. Recovery of sexual function remains poor. Stones and genitourinary sepsis are reduced.

5. Diffuse burning pain is a diminishing problem in well-managed cases. No

TABLE 23
ACTIVITIES

	Number Cases	Use Wheelchair	Use Braces	Use Crutches	Drive Auto	Walk Without Help	Confined to bed
Cervical	40	36	6	4	7	0	4
Dorsal	47	44	16	11	28	2	3
Lumbar	6	5	1	0	1	0	1
Cauda and conus	4	4	0	0	0	0	0
Cauda equina	3	3	0	1	3	1	0
Totals	100	92	23	16	39	3	8

chordotomies were needed in this series, nor was any dependence on narcotics or alcohol developed.

6. Spasms are still seen frequently, but they tend to diminish in time. No rhizotomies or obturator nerve sections were needed in the recent series.

7. Decubitus ulcers are fewer, smaller, and infrequently require plastic surgery now.

8. General physical state is excellent, weight loss low, blood chemistry normal, and anemia rare.

9. Recovery of motion and sensation remains the same as that of World War II, about 20 per cent. Autonomic system return is lower, 12 per cent.

10. Patients are up and active and only 8 per cent remain in bed, with attendant reduction in stones and associated genitourinary infection.

11. Morale of the new group is high, cooperation good, and there are no disciplinary problems.

12. Every phase of the paraplegia program, initiated in World War II and developed subsequently, must be carried out with unabated intensity. The principles are sound, but any lapse is promptly reflected in a regression of the patient's condition.

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CLINICAL PATHOLOGIC CONFERENCE

Raymond D. Adams, M.D.

Section Editor — with the assistance of E. P. Richardson, Jr., M.D.

Presented by Helena E. Riggs, M.D. and Charles Rupp, M.D.

CASE HISTORY

A young negro woman age 24 was admitted to the Philadelphia General Hospital on November 5, 1948, complaining of pain in the head, neck, and back. One week before admission, the patient had an acute episode of high fever (104° F.) associated with headache, vomiting, loss of sphincter control, and stiff neck. At this time she said she saw double and noticed her voice was hoarse. The fever yielded to antibiotic drugs over a period of two days. Until admission her temperature remained between 99° and 100° F. The past medical history shows that two years before the present admission, she was admitted to the hospital in coma with signs of meningismus. At that time, she was found to be in a crisis of sickle cell anemia. Liver damage was present and tuberculosis of the lymph nodes as well as pulmonary tuberculosis was present. She had also been hospitalized on several occasions for the treatment of anemia and tuberculosis.

Physical examination: The patient was a thin, confused, colored woman complaining of headache, with a temperature of 99.2° F. There was enlargement of the anterior and posterior cervical lymph nodes. The lungs showed poor expansion, with signs of cavitation at the left apex. The blood pressure was 100/80, pulse 80. The heart was enlarged, with the point of maximal impulse in the fifth interspace at the anterior axillary line, and a systolic murmur at the apex transmitted upward. The liver was enlarged 3 cm. below the costal margin.

Neurologic examination: The patient appeared to be disoriented; nuchal rigidity with positive Kernig and Brudzinski signs was present. Cranial nerves:—Enophthalmos and miosis was present in the left eye. Pupils reacted sluggishly both to light and accommodation. The fundus showed slight blurring of the disk margins. There was no exudate or hemorrhage. The left eye deviated inward at rest, and a slight ptosis of the left upper lid was present. Drooping of the left corner of the mouth was noted, as well as inability to wrinkle the forehead on the left. Hearing was impaired in the left ear for both bone and air conduction. The voice was hoarse. At times the patient had difficulty in swallowing and regurgitated fluids through her nose. Reflexes were decreased bilaterally but no abnormal reflexes were present. The patient staggered on walking and tended to walk to the left. Romberg sign was positive. Adiadokokinesis was present in the left upper extremity. The finger-to-nose and heel-to-knee tests were poorly performed on the left. There appeared to be hypotonia of the left arm and leg. The patient cooperated poorly in the sensory examination, but pain and temperature were definitely impaired over the right arm and leg and the left face. Touch, vibration, and position sense were retained. Barany test was unsatisfactory.

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Laboratory studies: The spinal fluid showed the following: pressure, 240 mm. of water; color xanthochromic; protein, 112 mg./100 cc.; cells—37 white cells, with 45 per cent polymorphonuclear cells, and 204 red cells. Serologic tests for syphilis were negative for both blood and spinal fluid. The red blood cell count was 1,480,000, with 99 per cent sickling; the white cell count was 6,500. Hemoglobin was 5 gm. Liver function tests gave the following results: thymol flocculation, 2+; cephalin flocculation, negative; thymol turbidity, 7.5. The blood sugar measured 61 mg. and the blood urea nitrogen, 10 mg.

Roentgenographic study of the lungs showed active tuberculosis, with a cavity at the left apex. Skull films were negative. The electrocardiogram showed an abnormal tracing consistent with a diagnosis of myocardial disease.

Course: The patient improved symptomatically over several days. Her headache decreased but she continued to complain of stiff neck and pain in the back. Spinal fluid studies were repeated and the presence of xanthochromic fluid confirmed. Spinal fluid protein continued to be over 100 mg./100 cc. and 25 white blood cells were present on the second occasion. Twelve days after admission the patient was found unconscious on the bathroom floor. She had apparently vomited, been incontinent of urine and feces, and had bitten her tongue. She recovered consciousness briefly, but lapsed into coma and died within 12 hours.

DISCUSSION

DR. MEYERS (student): I would say the patient had a sickle cell anemia crisis, with posterior inferior cerebellar artery thrombosis.

DR. FREY (student): She might have a mycotic aneurysm due to tuberculosis causing a spontaneous subarachnoid hemorrhage. The relapse following partial recovery suggests recurrence of subarachnoid hemorrhage.

DR. SCOTT (medical resident): My first choice would be tuberculous meningitis at the base of the brain, with involvement of the seventh and eighth nerves by meningeal exudate, and possibly a small tuberculoma in the distribution of the posterior inferior cerebellar artery in the medulla.

DR. TURNER (medical resident): I think the findings in this case can be explained on the basis of tuberculosis and its complications. The possibility of an aneurysm either congenital or mycotic cannot be ruled out.

DR. DELAPLAINE (neurologic resident): My first choice is subarachnoid hemorrhage into the posterior fossa due to sickle cell anemia, since spontaneous subarachnoid hemorrhage has been reported in this condition. There is a possibility of a posterior fossa abscess, with localized leakage into the subarachnoid space.

DR. RAY (neurologic resident): I do not think that one lesion explains all the findings. Sickle cell anemia can explain the majority of them, since focal cerebral vascular lesions occur in sickle cell anemia. However, I am more inclined to think that this patient had a miliary tuberculosis, with tuberculous meningitis and bulbar signs due either to a focal miliary lesion within the brain stem or to exudate around the brain stem. Horner's syndrome could be explained on the basis of tuberculous adenitis of the neck.

DR. BARROWS (neuropathologist): This young woman had symptoms suggesting a subarachnoid leakage which had come on precipitously about one week before. It is possible that the episode of meningismus two years before, when she was in coma, was an earlier attack of subarachnoid hemorrhage. In discussing the case, it might be wise to reverse the usual method of establishing the anatomic site first and to concentrate on the disease process. In any case of active tuberculosis, tuberculous meningitis is usually thought of in connection with meningeal irritation. However, fulminating onset of the meningeal symptoms within a few hours would be unusual, although possible, with rupture of a tuberculoma. Although the spinal fluid sugar was not determined, a tubercu-

lous meningitis producing such a profound change in the state of consciousness might be expected to show many more white blood cells in the spinal fluid. I would interpret the spinal fluid findings as due to hemorrhage.

This leads us to the several possible causes for subarachnoid bleeding: namely, aneurysms, intracerebral or intrapontine hemorrhage, or bleeding from a vascular malformation. I believe the neurologic findings point to a lesion of the brainstem. The hearing abnormality as well as the facial palsy suggests that the lesion may involve the cranial nerves after their exit from the substance of the pons. I would interpret difficulty in swallowing and fluid regurgitation as due to involvement of the corticobulbar fibers, although a primary nuclear palsy cannot be excluded. The weakness of the left arm and leg may be cerebellar, especially since we have no indication of reflex changes or presence of a Babinski sign. The patient had left-sided signs of cerebellar hemisphere involvement and probably involvement of the flocculonodular lobe. It is possible that the Horner's syndrome was due to compression of the superior cervical ganglion in the neck by the tuberculous nodes. To explain the presence of touch, vibration, and position sense, one must conclude that the medial lemniscus was not involved on either side.

I first considered that she had an intrapontine lesion, possibly a vascular malformation of the pons with hemorrhage. However, the loss of hearing on the left, the left facial palsy, and the left-sided cerebellar findings suggest that the primary lesion was outside of the medulla and compressed it to produce a left Horner's syndrome and hoarseness. Since the patient was sufficiently cooperative to allow a detailed sensory examination, the state of consciousness must have been fairly good, which does not support a diagnosis of intrapontine hemorrhage. Of the lesions adjacent to the pontomedullary junction which might produce lower cranial nerve palsy and ipsilateral cerebellar signs, carcinoma of the nasopharynx or chordoma are possibilities. Neither of these can explain the episodes of bleeding simulating subarachnoid hemorrhage, the last of which was fatal.

My diagnosis would be a congenital saccular aneurysm of the left vertebral artery at its origin from the basilar artery, which had leaked twice before and finally ruptured, or a mycotic aneurysm in the same site in a patient with sickle cell anemia. The more recent symptoms may be explained on the basis of increase in size of the aneurysm with compression of the restiform body, the seventh and eighth nerves, and the lateral surface of the medulla.

DR. RUPP (visiting chief of neurology): We have evidence that this patient had meningeal irritation. She gave a history of rather sudden onset of headache, vomiting, and stiff neck. She had positive Kernig and Brudzinski signs, and pain down the back of her legs. She also had slight blurring of the disk margins and a temperature of 104° F. at the onset of illness. In addition, she also showed evidence of a lesion in the pons and medulla. She had double vision, which probably was due to sixth nerve involvement since the left eye deviated in. She also had a left Horner's syndrome which could be due to the swelling in the neck, but more likely was the result of involvement of the central sympathetic pathway through the brainstem. She also presented evidence of peripheral seventh nerve involvement on the left and deafness in the left ear. She had a hoarse voice which could be due to involvement of the vagus nerve. She had left adiadokokinesia and left hemiasynergia which suggests involvement of the restiform body. She had crossed hypalgesia with involvement of the homo-

lateral face and contralateral trunk and extremities. She was said to have had weakness of the left arm and left leg, which is not usual in involvement of the posterior inferior cerebellar artery since the pyramidal tract is not supplied by that vessel. But, since she had no Babinski sign, possibly the weakness was more cerebellar hypotonia than a true motor deficit. These findings suggest a lesion in the distribution of the posterior inferior cerebellar artery, although in such cases the eighth and the seventh nerves are usually spared. This makes one wonder whether the lesion may be more peripheral to the area supplied by this vessel. As to the etiology, we know that the patient had active tuberculosis in her chest, and therefore one has to consider the possibility of tuberculous meningitis with an associated tuberculoma in the medulla.

Against the diagnosis of tuberculosis are the cerebrospinal fluid findings which were much more consistent with a vascular lesion. At onset she had a temperature of 104° F., but this dropped rather promptly with the administration of penicillin and sulfa drugs. In my experience the antibiotics are not so effective in controlling fever due to a tuberculous process. One gets the impression that after the first day or so she had a minimal temperature rise. A number of cases with bleeding into the subarachnoid space have had a rather high temperature at onset. Also in support of a vascular lesion are the abrupt onset and the rather sudden exodus. What is the vascular lesion? One has to consider the possibility of some malformation such as an aneurysm in the region of the posterior inferior cerebellar artery. This aneurysm was most likely extramedullary, in the region of the cerebellopontile angle, but one could conceive of it burrowing in or producing some vascular interference within the substance of the medulla and the lower pons. The patient had cardiac enlargement which is often associated with cerebral aneurysms.

One might consider the possibility of a malignant pontile tumor with hemorrhage into it. It is worthy of mention, but I do not think it likely, since all signs are on one side. Usually in tumors of the brainstem, there is involvement of both sides, and the motor symptoms rather than sensory ones are usually predominant. One might also wonder why the lesion would be so nicely limited to the area supplied by the posterior inferior cerebellar artery. The history of an antecedent episode several years before, with rather prompt recovery is against tumor.

One has to consider also the possibility that subacute bacterial endocarditis gave rise to an abscess in the medulla, but there is no definite evidence for this. The spinal fluid findings are certainly not suggestive of an infectious process.

Does the sicklemia play an etiologic role? I feel that it probably does. We know that two years previously she had meningismus in a sicklemic crisis. She was not too carefully studied at that time but one wonders whether she had blood in the spinal fluid at that time. Aneurysms may rupture during sicklemic crises. My final opinion is that the patient most likely had an aneurysm in the region of the posterior inferior cerebellar artery, with probably some extension of bleeding into the medulla and pons. Sicklemia is to be considered as a precipitating factor.

DR. RIGGS (neuropathologist): At post mortem this patient showed a massive terminal subarachnoid hemorrhage in the posterior fossa, with evidence of older bleeding, probably of a week or two duration. Along with that, there were very dense adhesions tying down the cranial nerves in the interpeduncular space and the nerves along the left side of the brainstem in the posterior fossa.

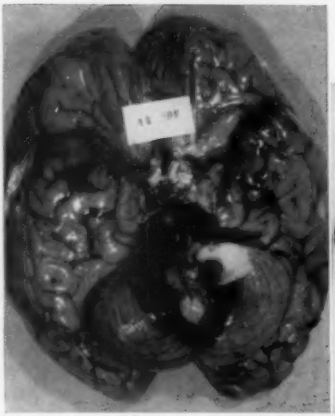

FIG. 1. *(left)* Ruptured miliary aneurysm at the origin of two medullary branches from the stem of the posterior inferior cerebellar artery.
FIG. 2. *(right)* Area of anemic infarction within the medulla in the distribution of the posterior inferior cerebellar artery.

This apparently was due to the hemorrhage that she had the year before. With difficulty, we dissected out an aneurysm which was bound down in the cerebellopontile angle and was very firmly adherent to all the cranial nerves on the left side below the seventh. It was a berry type of aneurysm with a narrow neck arising from the left posterior inferior cerebellar artery. In this patient the two vertebral arteries joined the basilar at the level of the pontomedullary junction. The aneurysm came off the posterior inferior cerebellar artery about one inch from its origin, at the bifurcation of two small branches supplying the medulla.

On microscopic study, we found an area of necrosis in the distribution of the posterior inferior cerebellar artery in the medulla. This was filled with macrophages. I would interpret the pathologic findings as follows:

This patient had a miliary aneurysm in a rather unusual location, namely on the posterior inferior cerebellar artery. It first bled several years ago as is shown by very dense adhesions around the base. A second episode occurred two weeks or more before death, again due to leakage from the aneurysmal sac. Finally at the time she was found unconscious, there was complete rupture. At the time of the second hemorrhage there was apparently sufficient disturbance in the circulation of the posterior inferior cerebellar artery distal to the aneurysm to cause the medullary lesion. It is very probable that the crisis of sickle cell disease was a precipitating factor in the leakage of the aneurysm.

DR. RUPP: Do you feel that this medullary involvement could be due to direct compression by the aneurysm rather than to interference with blood supply?

DR. RIGGS: I do not think I can rule that out. However, I have seen the medulla compressed by a large cerebellopontile angle tumor without focal necrosis of this type. This lesion is so clearly limited to the distribution of the artery that I would consider it due to disturbance in blood supply to this area, incident to the leaking of the aneurysm.

CASE REPORT

Tuberculous Spondylitis Simulating Herniated Intervertebral Disk

Harold Berris, M.D.

WITH increasing awareness of the syndrome of the herniated intervertebral disk, an ever greater number of patients are being subjected to lumbar laminectomy. It has long been recognized that many diseases may simulate a herniated intervertebral disk. Two cases are presented which point out the necessity for accurate diagnosis and demonstrate the serious nature of resulting complications.

CASE REPORTS

Case 1.—A 39 year old auto mechanic was admitted to the University of Minnesota Hospitals on July 6, 1952 with a three year history of low back pain and intermittent pain in the left leg in a sciatic distribution.

On physical examination the patient showed evidence of a recent weight loss. There was flattening of the lumbar lordosis, and straight-leg raising produced pain at 75° to 80° bilaterally. Sciatic notch tenderness was present on the left. No weakness, reflex, or sensory changes were noted. Routine urinalysis and hematologic studies were within normal limits. His temperature also was normal. A roentgenogram of the chest showed no pathology. A myelogram was done which showed a complete block of the subarachnoid space at the L4-5 level.

On July 7, 1952 a left hemilaminectomy at the L4-5 and L5-S1 level was done under general anesthesia. A cold abscess containing thick yellow pus was found. The disk material was biopsied. The pus was cultured and found to contain tubercle bacilli. The dura was penetrated during the procedure. Postoperatively the patient was placed on streptomycin, 2 gm. daily, and para-aminosalicylic acid 3 gm. four times daily. The patient improved and was discharged on July 19 after complete healing of the wound. He was instructed to continue the medications for one to two weeks. The pathologic report on the biopsy specimen was chronic granuloma, probably tuberculous, but acid-fast stains failed to reveal organisms in the tissue.

In spite of instructions, the patient did not continue taking the drugs after discharge from the hospital. Twelve days later he developed fever, headaches, nausea and vomiting, and disorientation. Three weeks later, on August 22, streptomycin and para-aminosalicylic acid administration was reinstituted.

On readmission to the hospital on August 31 the findings consisted of stupor, stiff neck, aphasia, early papilledema, bilateral abducens paresis, right lower facial paresis, and right hemiparesis. Repeated spinal fluid examinations revealed variations of the white cell count from 26 to 570, with mononuclear cells predominating. The spinal fluid sugar was as low as 24 mg. per cent, the spinal fluid chloride was depressed to a low value of 99 meq., and the protein increased to 102 mg. per cent. All of these returned to normal under therapy. Repeated cultures of the spinal fluid were sterile. A roentgenogram of the spine, which showed osteomyelitic involvement of L4 and L5 at the time of surgery, revealed sclerosis of the involved bones (figure 1).

The patient was treated with streptomycin intrathecally, dihydrostreptomycin intramus-

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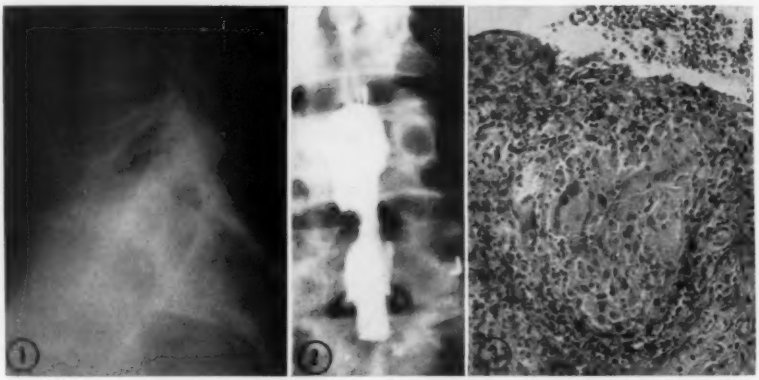

FIG. 1. Lateral view of the lumbosacral spine demonstrating bone destruction of the body of L 5 (case 1).

FIG. 2. Anteroposterior view of the myelogram in the lumbar area. Note the defect on the right at the L 4-5 level (case 2).

FIG. 3. Photomicrograph of the biopsy specimen demonstrating the granulomatous reaction in case 2.

cularly, para-aminosalicylic acid, and isoniazid. On this therapy the stupor cleared, aphasia gradually improved, but the right hemiparesis failed to improve. He was discharged to a sanatorium on April 10, 1953.

Case 2.—A 47 year old laborer was admitted to Minneapolis General Hospital on July 13, 1953 because of low back pain of several months' duration. Four weeks after onset he developed pain in the left leg along the sciatic distribution.

Examination showed some flattening of the lumbar lordosis and impaired straight-leg raising bilaterally. The chest roentgenogram showed a healed Ghon complex in the right lung. Urinalysis, serology, and routine blood studies were normal. A myelogram showed a defect on the right at the L4-5 level which was consistent with a herniated intervertebral disk (figure 2). On July 20 a laminectomy was done at the L4-5 level. At operation no herniation was found, but the L4-5 disk had a peculiarly gelatinous consistency. This was removed but the dura was not entered. Following surgery the patient had persistent low grade fever and complained of pain in the posterior part of the right calf. He was discharged on July 30 after his wound had healed.

Pain in the right leg became progressively more severe. The patient complained of anorexia, and on August 12, 1953 he developed frontal headache, nausea, and vomiting. On August 17 he was readmitted to the hospital with a temperature of 99.2° F. He appeared chronically ill. The liver was palpable two fingerbreadths below the right costal margin. Neurologic examination revealed blunting of the sensorium, stiff neck, weakness of the dorsiflexors of the right big toe, fasciculations, and decrease in tone of the right calf muscles. The right ankle jerk was absent. There was right sciatic notch tenderness, and straight-leg raising produced pain bilaterally.

The cerebrospinal fluid pressure was 320

TABLE 1

CEREBROSPINAL FLUID FINDINGS IN CASE 2

Date	*Source*	*Pressure*	*Color*	*Cell Count*	*% PMN*	*% Lymph.*	*Sugar CSF*	*Sugar Blood*	*Chloride*	*Protein*	*Pellicle*
8-19-53	lumbar	320	clear	58	14	86	44	134	—	—	—
8-20-53	ventricle	increased	clear	68	15	85	65		658	68	—
8-21-53	ventricle	—	yellow	520	25	75	48	72	648	52	—
8-27-53	lumbar	—	—	560	96	4	73		758	278	pos.
8-31-53	lumbar	—	—	122	6	94				304	

mm. of water. Spinal fluid findings are summarized in table 1. Following lumbar puncture the patient became rapidly more confused, and developed right pyramidal tract findings and irregular respirations. Because of this rapid progression, a right ventriculostomy was done (approximately 14 hours after lumbar puncture). The brain did not bulge through the dural incision, but fluid escaped from the ventricle under increased pressure. Streptomycin therapy by intramuscular and intrathecal routes was started on August 19, and the next day oral para-aminosalicylic acid and isoniazid were added to the therapy. On August 25 he developed a left hemiplegia, even though his mental status had improved. By August 29 he was alert and oriented. The hemiplegia showed signs of improvement by late September.

Microscopic examination of the disk material which had been biopsied showed chronic granulomatous inflammation with caseation consistent with a tuberculous lesion (figure 3). Cultures of the spinal fluid were negative for tuberculosis.

DISCUSSION

These two cases represent tuberculous lesions of the spine which produced symptoms and signs similar to a herniated intervertebral disk.

In case 1 the osteomyelitic lesion was clearly visible in roentgenograms of the spine. Tuberculous spondylitis most commonly produces a myelitic picture due to spinal cord compression, but since the lesion was at the L4-5 level, several segments below the lower end of the spinal cord, the clinical picture described was due to impingement of spinal nerves in the cauda. Tuberculous spondylitis rarely results in a secondary spread of the infection to the leptomeninges, but penetration of the dura at surgery may well have been a significant factor in the development of the tuberculous meningitis. It is of interest to note that antibiotics failed to halt its spread.

Case 2 demonstrates several interesting diagnostic and pathologic features. In this patient the defect in the myelogram, while quite consistent with that of a herniated intervertebral disk, was on the side opposite the radicular pain. On roentgenologic examination it was also noted that the bodies of the vertebrae adjacent to the involved disk showed minimal bone changes.

It has long been known that brucellosis and typhoid and paratyphoid fever may produce changes in the spine involving the intervertebral disk primarily. In addition to disk infections of specific etiology, there is also an entity of infectious spondylitis of undetermined etiology with little evidence of bone changes.[1] Turnbull[2] has recently reported three cases of disk infection following surgery for herniated intervertebral disk.

Tuberculous changes of the intervertebral disk have been considered as merely an extension of the process from adjacent vertebrae through defects in the cartilaginous plate. Cohn[3] has noted that destruction of the intervertebral disk occurs early in tuberculous spondylitis. The fibrocartilage and nucleus pulposus are the first structures to disappear, with relative sparing of the hyaline cartilage in the disk. The infection appears to extend from one body to the next by way of the longitudinal ligaments. Case 2 demonstrates this type of involvement.

Though the dura was considered to be completely intact in case 2, tuberculous meningitis resulted. The patient was readmitted to the hospital with a five day history of symptoms of meningitis.

SUMMARY

1. Two cases of tuberculous spondylitis simulating a herniated intervertebral lumbar disk are presented.

2. The pathogenesis of tuberculous spondylitis is clearly demonstrated in one of the cases reported.

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CASE REPORT

Coccidioidomycosis of the Central Nervous System

A Case of Ten Years' Duration

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Zondal R. Miller, M.D.

Coccidioidomycosis, a fungus disease caused by the organism, *Coccidioides immitis*, has been variously known as "San Joaquin Valley fever," "desert fever," or "California disease" over the past half century. It is generally conceded that its mode of transmission is by way of the spore form of the organism and is initially manifest as a respiratory disease.

It was described as early as 1892 by Wernicke and Posadas[1] as occurring in the Chaco district of South America, and later by Rixford and Gilchrist,[2] who were able to confirm its existence in the San Joaquin Valley of California. Little concerning the actual nature of the disease was known until 1935. However, Gifford and Dixon[3] were able to prove that this condition could occur not only in the familiar granulomatous form, but also as the common "San Joaquin Valley fever" long known in California. The problem of identification and treatment of coccidioidomycosis in all its forms became one of paramount importance with the coming of World War II, during which many Army training camps were established in California and contiguous endemic areas.

Doctor C. E. Smith of the Commission on Acute Respiratory Diseases of the Armed Forces Epidemiological Board made the following classification regarding the various manifestations of this condition:

1. *Initial or primary infection* (self limited, nearly always respiratory and focalized in the lungs)

   a. Inapparent or asymptomatic form (the usual type of infection which involves most residents of endemic areas).

   b. Acute respiratory, "influenzal" or "pneumonic" form (rarely diagnosed in civilian practice).

   c. Either of above types associated with erythema nodosum or multiforme (an allergic reaction frequently associated with joint and muscle pain known variously as "San Joaquin Valley fever," "valley fever," "desert fever," "desert rheumatism").

   d. Pulmonary cavity form (probably a

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complication of the acute respiratory type, cavity frequently closing spontaneously but sometimes persisting although infection is well focalized).

2. *Progressive,* "secondary," disseminated infection (usually fatal, known as coccidioidal granuloma, chronic granulomatous coccidioidomycosis, "San Joaquin Valley disease," "California disease").[4]

There are many excellent and detailed reports in the literature concerning the pathogenesis, epidemiology, and clinical manifestations of this disease, particularly that of Schwarz and Muth in 1951.[5] Less can be found, however, concerning the neurologic complications of coccidioidomycosis, one form of the disseminated infection.

Smith[6] and his associates in 1946 analyzed a series of 1,351 cases of coccidioidal infection encountered over a four year period, discovering that 60 per cent were asymptomatic while 25 per cent were diagnosed clinically. Erythema nodosum occurred in 4.6 per cent, but disseminations occurred in only 1 per cent of the clinically manifest infections encountered in white males. Forbus,[7] however, collected 95 cases of the disseminated type occurring in the Army during World War II and discovered 10 per cent of those cases had nervous system involvement confined to the meninges.

Other reports regarding disseminated coccidioidomycosis indicate that meningeal involvement is relatively more common. Schlumberger[8] produced evidence from Army Institute of Pathology records showing a basilar meningitis in 13 of 23 cases of disseminated coccidioidomycosis coming to autopsy. Curiously, the picture of meningitis may often be the only symptomatology demonstrated by the patient, the initial pulmonary invasion having been so slight as to have been forgotten. All authors are in agreement that the prognosis in cases of disseminated coccidioidomycosis is very grave, particularly when there is nervous system involvement. In no case reported to date has there been survival beyond four years and eight months.[9]

Our intent in reporting this patient is to present the longest known survival of a proved case of coccidioidal meningitis, and also to review briefly the surgical procedures employed as palliative measures for relief of symptoms arising out of chronic increased intracranial pressure and the rehabilitation measures provided the patient to make an extra-hospital environment feasible for him.

CASE REPORT

The course of this white male's disease dates from February 1944, when he was hospitalized for ten days with "acute catarrhal nasopharyngitis" while training with his Army unit on the Mojave desert. Army records of studies done at that time reveal that a chest roentgenogram and all laboratory examinations were considered to be within normal limits.

While serving in Europe in August 1944, he began experiencing intermittent nondisabling frontal headaches. He was not seen by a medical officer until hospitalization for a shrapnel wound of the knee in October 1944. Examination then revealed bilateral papilledema.

Spinal fluid examinations in December 1944 revealed the presence of "coccidioides-like bodies" on smear. Repeated chest films were normal, sputum examinations for *C. immitis* were negative, and the coccidiodin skin test was also negative. The following month a ventriculogram was done, showing only a slight dilatation of the lateral ventricles. This was followed a month later by pneumoencephalography which, in addition to the previously discovered dilatation, revealed a slight shift of the ventricular system to the left. A tentative diagnosis of chronic arachnoiditis was then made.

In the succeeding months repeated lumbar punctures were done. The findings are summarized in table 1.

By May 1945 the patient was virtually asymptomatic except for occasional headaches. Neurologic findings at that time revealed a chronic bilateral papilledema of 3 to 4 diopters, absent right patellar reflex, and bilaterally absent ankle reflexes. Cultures and smears of blood and spinal fluid were persistently negative but a coccidioidin

TABLE 1

CEREBROSPINAL FLUID DETERMINATIONS IN A CASE OF PROVED COCCIDIOIDOMYCOSIS OF THE NERVOUS SYSTEM

DATE	Dec 27 1944	Dec 29 1944	Jan 10 1945	Jan 14 1945	Jan 16 1945	Apr 5 1945	Apr 17 1945	Apr 24 1945	May 29 1945	Oct 1 1945	Mar 1 1948	Mar 17 1948	Dec 3 1948	Jul 31 1951	Mar 4 1953	Mar 19 1953	Apr 30 1953	Feb 10 1954
White blood cells	401	337	131	3530	450	620	697	679	430	521	130	410	255	240	267	860	—	31
Polymorphonuclear cells	15	8	10	71	15	3	21	20	61	9	34	40	50	6	24	33	—	16
Lymphocytes	85	92	80	29	70	86	78	78	36	91	66	60	50	94	76	67	—	84
Eosinophils	—	—	—	—	10	11	1	2	2	—	—	—	—	—	—	—	—	—
Sugar (in mg. %)	—	—	56	15	21	24	40	—	46	—	28	44	26	—	27	17	56	43
Protein (mg. %)	—	168	102	180	96	193	179	—	240	207	330	280	270	—	143	650	202	128
Colloidal gold	—	5554 221 000	—	—	—	0000 000 000	—	—	0000 000 000	1111 122 210	5555 554 321	5555 543 320	5555 543 321	3211 100 000	—	—	—	5555 332 100
Pressure (in mm. water)	230	320	—	—	—	300	420	—	—	—	—	—	230	—	450	—	600	—

skin test was found to be 1 plus at 24 and 48 hours.

A blood sample was sent to Doctor C. E. Smith at that time; his report on the complement fixation and precipitin tests confirmed the diagnosis of coccidioidomycosis. Repeated efforts were made to obtain consent of the patient for a palliative ventriculovenostomy, but he refused and was discharged from the service in October 1945.

During 1946 and early 1947 the patient worked in various clerical jobs while attending law school. Except for periodic refractions for eye glasses he apparently got along well. He was first seen as an outpatient by the neurologic department of the Minneapolis Veterans Administration Hospital in March 1947, at which time his only complaints consisted of occasional headache, lack of coordination on walking upstairs, and nervousness. Neurologic examination disclosed chronic bilateral papilledema, minimal ataxia, and the reflex changes described previously.

In January 1948, he was first admitted to the Minneapolis Veterans Administration Hospital after he had had two episodes of unconsciousness which observers told him were similar to epileptic seizures. He also complained of periodic dizziness, especially on sudden movements of his head. The neurologic examination revealed no change. Roentgenograms of the skull revealed an increased depth and anteroposterior lengthening of the sella turcica. All laboratory studies with the exception of the spinal fluid examination were within normal limits. The visual fields were normal. However, guinea pig inoculation and culture of spinal fluid revealed *C. immitis*. No seizures were observed during hospitalization and he was discharged without further treatment.

By December 1948 the patient began to complain of periodic episodes of amnesia lasting up to three hours. In addition, he had also been observed by relatives to stand for long periods of time staring blankly. Examination again revealed no significant change, although the electroencephalogram was reported as mildly abnormal, with diffuse slowing evident.

He was discharged on anticonvulsant medication and followed for a year as an outpatient with no change in either symptoms or findings, except that no further seizures were noted.

He was readmitted in July 1950, following an episode of transient blindness of the right eye. The patient's memory for recent events was markedly impaired. Examination revealed a chronic papilledema, enlarged blind spot on central fields and constriction of the peripheral fields, nystagmus on right lateral gaze, poorly performed tandem gait, and minimal bilateral upper extremity incoordination. The electroencephalogram was again interpreted as mildly abnormal. During this hospitalization the patient awakened several times at night and wandered about in a confused state. No new therapy was instituted and he was discharged to be followed in the neurologic outpatient department.

There was no further change until February 1953, when he again presented himself with complaints of increasing memory deficit, "shaky spells," and failing vision. He was admitted at this time for consideration of some type of surgery to shunt the flow of cerebrospinal fluid and provide better absorption.

Neurologic examination on this admission revealed the previously observed bilateral chronic papilledema, right lateral nystag-

mus, poor balance and gait, minimal adiadokokinesis, decreased right patellar reflex, and absent ankle reflexes. Skull roentgenograms revealed no change from previous examinations, routine laboratory procedures were within normal limits, but lumbar puncture revealed a pressure of 450 mm. of water. A culture for *C. immitis* was found to be negative.

In view of the patient's evident increasing deterioration, secondary to chronic elevation of intracranial pressure, a right ventriculovenostomy was performed, with marked improvement apparent a few days postoperatively. Lumbar puncture on March 19, 1953 revealed a pressure of 220 mm. of water. Phenolsulphthalein tests showed an excretion of 17 per cent four hours after the injection of dye into the spinal canal, and 67 per cent total excretion after ten hours.

At that time the patient stated that his vision was better and he improved sufficiently to be allowed a 30 day leave of absence, but on April 30, 1953 he was brought to the hospital in a semiconscious condition. The patient's wife reported that he had been having repeated mild seizures, was markedly deteriorated in behavior, and seemed critically ill. Examination revealed that the trephine holes were bulging, and a ventriculostomy was performed as an emergency measure. The ventricular pressure was found to be well over the 600 mm. limit of the water manometer. It was presumed that the ventriculovenostomy performed previously was no longer functioning.

During the following week the patient's condition remained critical and a Torkildsen procedure was then performed without apparent immediate effect.

For the next five months the patient was kept in the hospital in a virtually vegetative state. He had transient lucid periods, but then lapsed into a lethargic state punctuated by bouts of nausea and vomiting. Frequent attempts were made to ambulate him, but at no time was he able to sit alone in a chair or walk without the assistance of two attendants.

By mid-October 1953, however, it became apparent that the patient was spontaneously attaining some precarious balance in the absorption of spinal fluid. Psychometric evaluations were performed but were limited sharply by the marked visual deficit. These revealed that, while the patient had previously had an intelligence quotient of 131 as measured by the Shipley-Hartford intellectual screening test in March 1953, he was now at a level of 95 on the Wechsler-Bellevue scale.

Upon completion of these studies he was placed on the corrective rehabilitation service where he was given an intensive program of muscle strengthening, coordination, and walking exercises. Within a month under this regimen he was able to ambulate alone, walked up and down stairs with the assistance of a side rail, and was able to take care of all bodily needs. After a trial leave during which he was able to help his wife with simple duties and do errands outside the house, he was discharged on February 15, 1954, approximately ten years from the date of onset of coccidioidomycosis. At no time has he shown evidence of other system involvement.

DISCUSSION

While coccidioidomycosis has been recognized as a disease entity for over 60 years, its diverse manifestations, particularly with regard to the nervous system, have not been studied extensively, chiefly because of the short survival span when such dissemination occurs. So far as we are able to ascertain the patient reported here represents the longest survival period observed in a case of proved coccidioidomycosis. Further, this appears to be the only instance in which repeated palliative surgery was successful to the extent that the patient, although severely disabled, has survived and has been rehabilitated sufficiently to allow discharge to the home.

SUMMARY

A case of disseminated coccidioidomycosis followed over a ten year period is presented. It was manifested by chronic meningitis and presumed adhesive arachnoiditis, with chronic increased intracranial pressure, visual disturbance, seizures, staggering gait, and mental deterioration. During the past year this patient was subjected to ventriculovenostomy and ventriculocisternostomy, after which an apparent balance in reabsorptive function of spinal fluid was established and sufficient improvement resulted to permit rehabilitation and eventual discharge.

The cooperation and suggestions of Doctor C. E. Smith of the Commission on Acute Respiratory Diseases of the Armed Forces Epidemiological Board are gratefully acknowledged.

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The convulsions which occur as a result of chronic brain disease may be divided into two classes: (1) Those which are the result of organic disease, such as can be recognized, after death. (2) Those which are the expression of a condition of the brain which is not evidenced by any visible alteration. The only evidence of disease being the disordered function, they are termed "functional" diseases.

The object of this work is to consider the clinical history of the chronic convulsive diseases of the latter class; which depend on such conditions of the nerve centres as elude detection by the methods of examination at present at our disposal. In considering these diseases it will, however, be necessary to refer to many facts relating to the organic diseases of the brain. There is, moreover, one class of convulsions due to organic brain disease which it has seemed well to consider more fully, namely, those which succeed an attack of hemiplegia from which a more or less complete recovery has taken place.

The chronic convulsions which are recognized as of "functional" origin are commonly divided into two classes – the epileptic and hysterical attacks. The former are characterized by almost invariable loss of consciousness and special forms of spasm, tonic or continuous, clonic or intermitting. In severe attacks (epilepsia major, *grand mal*) both forms of spasm usually occur. The muscular contractions are of violent random character, fixing the limbs in unnatural attitudes, unlike those which are assumed during voluntary movements. In slighter attacks (epilepsia minor, *petit mal*) there is transient loss of consciousness with little or no convulsion. In some rare attacks (less common than in cases of actual organic disease) there is slight convulsion without loss of consciousness.

W. R. Gowers in *Epilepsy and Other Chronic Convulsive Diseases*, published in 1885.

CASE REPORT

Total Left Cerebral Hemispherectomy for Malignant Glioma

William F. Hillier, Jr., M.D.

A SURVEY of the literature reports some 41 hemispherectomies,[1–8] 28 of which have been done in this country. Of this number four left hemispherectomies are cited. One of these was performed in 1934 for a malignant tumor with a survival of 17 days, with death due to meningitis.[1] Another carried out in 1949 was reported to have a survival of four months. The only other cases of total left hemispherectomy in the literature are two cases performed for infantile hemiplegia, and both patients are still living and apparently well.[3] Therefore it would appear that total left hemispherectomy for malignant brain tumor has had discouraging results.

The report of Bell and Karnosh[4] gives an excellent picture of a 10 year survival following a right cerebral hemispherectomy. The present case is reported as a 27 month survival of a young man with a recurrent glioma involving the posterior half of the left cerebral hemisphere.

CASE REPORT

A 14 year old Indian boy from the Cherokee Indian Reservation in Cherokee, North Carolina, was seen for the first time on January 3, 1951. The history obtained from the parents revealed that four months prior to examination the patient began to complain of headache, nausea, and vomiting. These symptoms were transient at first but had progressed in both frequency and severity. During the two weeks preceding this examination, he had complained of double vision and blurring of vision.

Examination showed a well developed and well nourished young man who appeared to be acutely and severely ill; he was rather drowsy, somewhat confused, and exhibited a pronounced degree of motor aphasia. He made every effort to cooperate, and the examination was fairly satisfactory. The head was negative to percussion and auscultation. No bruit was heard. The pupils were round, regular, and equal, and they reacted equally to light both directly and consensually. Accommodation could not be tested adequately. On confrontation testing there was a definite right temporal and left nasal visual field defect. There was papilledema of three diopters bilaterally. There was a right central facial weakness and a slight degree of weakness of the right hand and arm. No sensory changes were observed. The reflexes were present, active, and equal bilaterally. No pathologic reflexes were detected. It was felt that the patient had a brain tumor in the left occipitoparietal region, and he was immediately transferred to the hospital where skull roentgenograms failed to reveal any significant changes. The sella turcica appeared to be

From the neurosurgery service, Memorial Mission Hospital, Asheville, North Carolina.

normal and there was no evidence of erosion of the posterior clinoid processes.

A ventriculogram was performed, and upon insertion of a left ventricular needle, 45 to 50 cc. of cystic fluid under markedly increased pressure was obtained. This fluid contained 27,250 red blood cells per cu. mm., and had a protein content of 325 mg. per cent. The right ventricular needle encountered crystal clear fluid under markedly increased pressure; there was obvious displacement of this ventricle to the right. No communication could be demonstrated between the large left cystic cavity and the right lateral ventricle. Good filling of the cystic cavity was obtained, and air was inserted into the right lateral ventricle. Ventriculograms revealed a large cyst-like structure in the left occipital region which appeared to cross the midline, and there was a small secondary cyst arising from its posterior aspect. The right lateral ventricle contained very little air and was displaced markedly to the right. The roentgenologic impression was that of a space-occupying, cystic lesion in the left occipitoparietal region.

A craniotomy was performed through a large occipitoparietal bone flap. The dura was exceedingly tense and bulging. A ventricular needle was inserted into the cystic structure and 50 cc. of orange-red fluid and air were evacuated. The dura was then opened, and the brain was found to be tense, with marked destruction of the vascular pattern on its surface. At a depth of 3.5 cm. a bluish cyst wall was encountered, and dissection was carried out around this cystic structure. On proceeding about the circumference of this cyst, a firm mass could be seen in the cyst wall suggesting a large mural nodule. It was possible to obtain a moderately good cleavage plane around this cystic structure, and the tumor was removed without undue bleeding. There was a considerable amount of cerebral edema, and the closure was carried out with some difficulty after the administration of 50 cc. of 50 per cent dextrose.

The patient's postoperative course was satisfactory for the first five days, when he developed a low-grade fever due to a urinary tract infection; this responded satisfactorily to appropriate drug therapy. He was permitted up on the tenth postoperative day and discharged on the fourteenth postoperative day. At the time of discharge he had persistence of the previously mentioned visual field defect, motor aphasia, right central facial weakness, and a spastic type of paresis in the right arm. Histologic examination revealed the tumor to be an astrocytoma.

The patient was seen at regular intervals and resumed most of his normal activities. In April 1951, following a period of square dancing, he again began to have nausea, vomiting, and headache. Over the next four weeks he noted some degree of mental confusion, progression in severity of the aphasic defect, and pain in the right leg. Examination on May 1 revealed the bone flap to be elevated, and there was early papilledema and a fairly definite central facial weakness. The aphasia was much more pronounced and of a mixed type, with more marked sensory elements than motor. There was weakness of both the right arm and leg. The reflexes were hyperactive in the right arm and leg.

It was felt that there was a recurrence of the tumor, and on May 8 a left parietooccipital craniotomy was performed. The dura was tense. The brain was tight and bulging. A ventricular needle was inserted with the release of a large amount of yellow fluid. Upon opening the dura, a firm rubbery yellow tissue was noted at the posterior inferior margin of the exposed area. In addition to solid tumor, there was a cystic mass about the size of a lemon. Dissection proceeded along good cleavage planes, but below the cyst there was a large mass of reddish-grey, fairly firm tumor tissue extending deep into the parietal and temporal lobes. The major portion of this tumor tissue was removed, with an effort to leave as much normal brain undisturbed as possible. At operation the surgeon felt that the picture was that of a malignant glioma, probably a glioblastoma multiforme. Histologic examination revealed the tumor to be a malignant glioma, type undifferentiated.

On the sixth postoperative day a persistently high temperature together with an elevated cerebrospinal fluid pressure suggested an extradural hematoma, and the flap was reopened. No hematoma was detected, but a large amount of old blood and cerebrospinal fluid was found in the tumor bed. This was evacuated, and after meticulous hemostasis, closure was carried out in the usual manner. The patient was discharged on the thirteenth postoperative day.

The neurologic examination at the time of discharge revealed homonymous hemianopsia, right central facial weakness, right spastic hemiparesis, and mixed aphasia. The

patient was followed at appropriate intervals, and he progressed satisfactorily until July 15, at which time the parents reported some puffiness over the operative areas and a discharge of yellow pus from the posterior inferior margin of the wound. Culture revealed hemolytic *Staphylococcus aureus*. The patient was admitted to the hospital and, under massive doses of Crysticillin for four days, there was prompt clearing of the discharge and healing of the wound.

The patient's course was followed periodically. He made progressive improvement, with marked clearing of the aphasic defect; he resumed normal activities for a boy of his age. In April 1952 the parents reported that he again began to complain of headache, nausea, and vomiting, with increase in weakness, spasticity of the right side, drowsiness, mental confusion, and very severe aphasia. The neurologic examination at this time revealed the operative site to be tense and bulging. The occipital burr holes were full and protruding. There was profound papilledema, and the patient was extremely drowsy and responded little to questioning. The reflexes of the right arm and leg were decidedly hyperactive. The patient's condition appeared to be critical.

After careful discussion with the parents, with adequate explanation of the permanent defects likely to follow total hemispherectomy, this operation was performed on April 13, 1952. After exposing the old operative site through a very large occipitoparietal bone flap, a tremendous recurrence of the tumor could be seen involving the occipital and parietal lobes and a large portion of the temporal lobe. Hemispherectomy was then carried out, sparing as much of the basal ganglia as possible. The patient's immediate postoperative course for some eight hours was stormy, but then stabilized more satisfactorily. There was a rapid flattening of the temperature curve.

The patient at first had a complete spastic hemiplegia, was unable to speak, and was unable to swallow. He was maintained on tube feedings for ten days and then was able to take liquids without difficulty. On the seventh postoperative day the sutures were removed, revealing a well healed wound. By the sixteenth postoperative day the patient was able to say, "mother," "father," "nurse," and similar expressions. At this date also, he was moving his right arm and leg, and by the eighteenth postoperative day he was up in a chair. He was able to take a few steps on the twentieth postoperative day and had already regained considerable strength in the right arm and leg. Because of the difficulty in following such a patient at a great distance from the hospital, he was kept for 36 days. At the time of his discharge he was as cheerful and alert as prior to operation. He appeared to have perfectly normal powers of comprehension of the spoken word and appeared to enjoy music considerably. He was able to eat all foods without difficulty. The papilledema had receded. There remained the previously mentioned visual field defect, a minimal right central facial weakness, and a right spastic hemiparesis which was gradually improving. There were hyperactive deep tendon reflexes of the arm and leg, with positive patellar and ankle clonus on the right. There was no Hoffmann sign. There was some hyperalgesia over the right side of the face, but sensation over the arm and leg showed little difference from that on the left side. The patient's vocabulary showed daily improvement though he had a tendency at first to respond to questions with, "I don't know"; persistent questioning, however, resulted in appropriate responses. He was able to call his physician and nurses by their names. He was possibly slightly euphoric.

The patient has been followed for 27 months postoperatively, and is now capable of walking with a short leg brace, but without other assistance. He does not tend to swerve or stagger, though he has a definite weakness of the spastic variety in the right leg, with persistent patellar and ankle clonus. Flexion and extension of the right arm are well performed. There is little or no function in the right hand. The facial weakness on the right has entirely disappeared. Accurate visual field testing reveals a preservation of macular vision with the homonymous hemianopsia. Comprehension of the spoken word is quite accurate. The motor aphasia shows a constant improvement. He is capable of reading individual letters, but cannot formulate words. He is at times unable to name an article in an advertisement, but yet can tell the radio program and describe the artists who advertise the particular product.

Recently the patient again exhibited drowsiness and mental confusion and had several severe focal convulsive seizures localized to the right arm and leg. He rapidly developed status epilepticus, which was controlled by general anesthesia. His temperature reached 105° F. Repeated spinal punc-

tures showed crystal clear fluid with no cells but an increased pressure and a protein varying from 55 to 78 mg. per cent. Two days later puffiness of the scalp suggested a collection of fluid, and subgaleal aspiration obtained 120 cc. of yellow pus which cultured a hemolytic *Staphylococcus aureus*. With the administration of Terramycin and repeated subgaleal aspirations, this abscess is clearing rapidly. Spinal fluid findings remain normal. The patient is afebrile, ambulatory, and has returned to his level of performance prior to this most recent episode.

CONCLUSION

A case of total left hemispherectomy is reported, that of a young man in whom the entire left cerebral hemisphere was removed for malignant glioma. There has been no evidence of recurrence of this neoplasm in the right cerebral hemisphere after 27 months. The neurologic deficit is much less severe than would be anticipated from removal of the dominant hemisphere in a right-handed individual. There is evidence to suggest a strong transference of left hemispheral functions to the remaining right cerebral hemisphere. The procedure certainly is justified only in certain selected cases, but it would appear that the criterion for selection might be more broad than has been previously described. The patient dealt with in this report is an enthusiastic young person with a markedly out-going personality, and perhaps these qualities plus an unswerving devotion on the part of his parents have made possible the results described.

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Neurology BOOK REVIEWS

Essentials of Neuropathology

Cyril B. Courville, M.D. 1953. Los Angeles: San Lucas Press. 264 pages, $6.50.

With medical school curricula bulging at the seams as they now are, even the most exacting teachers will admit that it is becoming increasingly necessary to restrict the presentation of any field to its guiding principles, its main facts, and its most obtrusive unsolved problems. The author's purpose in writing this small book was to compose just such a primer of neuropathology, designed expressly for the use of undergraduate medical students. In many ways this is a much more difficult assignment than compilation of a comprehensive reference work.

As would be expected, Dr. Courville's approach to this book is based upon his well-known textbook, *Pathology of the Nervous System*. The organization, the viewpoints, and the emphasis in the two books are the same. But the smaller book is not a mere digest of the larger; in many particulars the text has not only been condensed but also rewritten with the needs of the medical student in mind.

In his selection of what is important Dr. Courville has been guided by the frequency with which he has encountered disease processes of the nervous system in the vast autopsy material of the Los Angeles County Hospital. In the main this works out very well. Well over half of the book is devoted to vascular lesions of the brain, pyogenic and granulomatous infections of the nervous system, traumatic lesions, and tumors. The treatment of these topics is pointed, interesting, and often original. The morgue of a large public hospital is not, however, a reflection of the neurologic clinic nor even of the office of the general practitioner.

Moreover, the author's concern "to cut away some of the underbrush," as he puts it, has led him to prune too far at times and has left some of the branches much too bare. For example, the only mention of the pathology of paralysis agitans is a statement to the effect that the disease is believed to result from impaired circulation of the corpus striatum. Amyotrophic lateral sclerosis appears only as a name in a classification, and syringomyelia is given merely passing mention in connection with malformations of the spinal cord.

Many excellent examples of gross brain lesions are illustrated by photographs from the author's extensive collection. Unfortunately the microphotographs often fail to depict the lesions well because of faulty reproduction or excessive reduction in size.

R. B. R.

NEWSLETTER

SEPTEMBER, 1954

Howard D. Fabing, President
Walter O. Klingman, President-Elect
Francis M. Forster, Vice-President
Alexander T. Ross, Secretary
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AMERICAN ACADEMY OF NEUROLOGY

AAN Committee on Nomenclature Defines Activities At the annual meeting of the Academy in Washington, D. C. (April 26-May 1), the Committee on Nomenclature and Biometrics (formerly the Committee on Epidemiology), chaired by Lawrence C. Kolb, defined its functions and responsibilities. Among them: provide statements on the frequency and distribution of neurologic disorders; initiate statistical and epidemiologic studies in neurology and assist in the promulgation of such studies; assist voluntary health societies in the preparation of estimates of the prevalence and distribution of these disorders; and formulate appropriate genetic studies in this field.... The committee also will review and study current usage of neurologic nomenclature and suggest appropriate changes to such organizations as the National Office of Vital Statistics, the American Medical Association (for use in its standard nomeclature), etc..... The national offices of voluntary health agencies dedicated to specific neurologic diseases will be informed of the existence and function of this committee.

Brown Comments on Norwegian Neurology An important unreported stage in the neurologic peripatetics of Joe R. Brown, abroad last summer (see February and April, 1954 Newsletters), was his visit to Norway. Starting in Oslo, he visited Dr. Jan Jansen of the Institute of Anatomy, and discussed the latest anatomic studies on the cerebellum with particular reference to the relationship of the paraflocculus of the whale to the functions of the truncal musculature. He also had the opportunity of visiting the neurophysiology laboratory where electromyographic studies were being pursued on the functions of the gamma fibers which innervate proprioceptive end-organs. Next Brown visited the neurologic unit of Prof. Monrad-Krohn, an international figure of great eminence who visits the U. S. A. every 25 years (last visit in the spring of 1954). Prof. Monrad-Krohn and his staff are actively pursuing studies on the residuals of cerebral anoxia and neurologic language disorders. According to Brown, the neurologic unit at Oslo is well balanced with diagnostic and treatment facilities for acutely ill patients, as well as general out-patient service and a special epilepsy follow-up unit. Prof. Monrad-Krohn

also has developed a rehabilitation service for neurologic patients and proudly showed his rehabilitation gymnasium. A new building for neurology is now under construction.... From Oslo, Brown proceeded to the University of Bergen, where the Hansen bacillus was discovered and where much of the early research in leprosy was carried on. Here he spoke to the head of the neurologic unit, Dr. Sigvald Refsum, who has spent several years in the United States and is well known to many American neurologists.... In Norway, there are 37 certified neurologists, four certified neurosurgeons, and about 11 neurologists in training. The neurologic training includes one year of general practice, one year of internal medicine and surgery combined, one half year of psychiatry, and three years of neurology. Basic science training is acquired along with experience in clinical neurology.

Wartenberg Acclaimed In Belgrade Eleanor Little, editor in the department of neurology, University of California, has forwarded a translation of a news item from a Belgrade newspaper (July, 1954), reporting on the visit of Robert Wartenberg to Yugoslavia as guest of the Serbian Medical Society and the Medical Faculty in Sarajevo. Dr. Wartenberg, who conferred with neurologists there, is acknowledged as a "scientist of world renown," and much space is devoted to his achievements in the field of clinical neurology. The Belgrade paper also notes with pride that Wartenberg agrees with their physicians in maintaining that the Lasegue sign was not discovered by Lasegue but by the Serbian physician and writer, Laza Lazarevic, and they express the hope that this will lead to acknowledgment of the Lasegue sign as the Lazarevic sign.

* * * * * *

Neurosurgical Congress to Be Held at Montevideo AAN members have been invited to participate in the 6th Latin-American Neurosurgical Congress to be held in Montevideo, Uruguay, from March 21-25, 1955. The program includes a symposium on the thalamus, as well as the problems of brain herniations, pain surgery, and dyskinesias. A large attendance from the United States is anticipated. Abstracts of papers should be sent not later than January 1, 1955, and complete papers before March 1, 1955, if they are to be published in the transactions of the Congress. All communications should be forwarded to the General Secretary of the Congress, 1287, Montevideo, Uruguay.

Institute of Neurological Sciences Established at Pennsylvania The new Institute of Neurological Sciences, recently established under the directorship of Dr. Louis B. Flexner, began operations on July 1. The purpose of the institute is to provide a center for basic training in the neurologic sciences, particularly neuroembryology, neuro-

anatomy, neurophysiology, neuropharmacology, neurochemistry, and experimental psychology. Its goal is to make feasible interdisciplinary research training through on-the-job experience in research. Accordingly, in addition to didactic seminars, the program provides for research assistants and fellows to rotate through the laboratories of at least two of the five basic neurologic disciplines represented.... Training at the Institute is open to a limited number of adequately prepared candidates for the degree of doctor of philosophy; to certain qualified medical students; and to postdoctoral investigators (Ph.D. or M.D.) wishing advanced training for a research or clinical career. Fellowships are also available for postgraduate investigators, again Ph.D. or M.D., the stipends to be arranged according to need. Degrees will be awarded by the department in which the research thesis is undertaken, not by the Institute.

National Foundation Clinical Fellowships The National Foundation for Infantile Paralysis has announced sponsorship of one year clinical fellowships to train physicians in various aspects in the total care of the poliomyelitis patient. Candidates for these fellowships must be United States citizens (or applicants for citizenship) and must have completed at least one year of internship in a hospital approved by the Council on Medical Education and Hospitals of the American Medical Association. Before applying for a fellowship, the candidate should arrange for a program of full time study in any institution having suitable facilities for this type of training. Stipends range from $300 to $400 a month, depending upon marital status and number of dependents. Applications for fellowships received before September 1 will be considered in November; those received by December 1 will be considered in February; those received by March 1 will be considered in May. Selection of condidates will be made on a competitive basis by the National Foundation's Clinical Fellowship Committee.... For application forms and further information, communications should be forwarded to the National Foundation for Infantile Paralysis, Division of Professional Education, 120 Broadway, New York 5.

Glock New President of MS Society The National Multiple Sclerosis Society announces the election of Ralph C. Glock as president of the society. Mr. Glock is vice-president of the Bank of New York and has long been interested in the work of the society. William C. Breed, Jr. of New York, whose activities in the society date back to its inception seven years ago, has been elected chairman of the board of directors. The society also announces the appointment of Judson Miles Rees, formerly director of public relations for the United Hospital Fund, as associate director.... The National Multiple Sclerosis Society now has 47 chapters throughout the country

dedicated to the finding of the cause and control of multiple sclerosis and related neurologic disorders. The society's central office is at 270 Park Avenue, New York 17.

Tiffany Lawyer to Head Neurology at Montefiore Tiffany Lawyer, Jr., currently associate professor of neurology at Georgetown University Medical School, has been appointed chief of the neurology division of Montefiore Hospital in New York, assuming the post recently vacated by T. J. C. von Storch. Prior to coming to Georgetown in 1952, Dr. Lawyer, a graduate of Albany Medical College, had been an associate in neurology at Columbia University and adjunct attending neurologist at Montefiore Hospital, as well as chief of the neurology section of the Veterans Administration Central Office. Filling Dr. Lawyer's position at Georgetown is Dr. Desmond O'Doherty, previously instructor in neurology and head of the Georgetown Neurology Service at D. C. General Hospital (formerly Gallinger Municipal Hospital).

Briefs President Howard D. Fabing will present his plans for reforming state laws on epileptics before the Western Institute of Epilepsy at their meeting in Galveston, Texas (October 22). The day before, he will address the medical students at Baylor University Medical School and make a preliminary survey of the facilities of the Shamrock Hotel in Houston, the site selected for the annual AAN meeting in 1955.... A. Theodore Steegmann, Academy historian, requests all members to forward any news clippings, photographs, or other interesting material from previous meetings, which are needed for the files of the history committee. This material should be forwarded to Dr. Steegmann at the University of Kansas Medical School, Kansas City 3.... Papers presented on the status of multiple sclerosis at the conference of the National Multiple Sclerosis Society and the New York Academy of Sciences (April 17-18, 1953) have been published in the Annals of the New York Academy of Sciences (Vol. 8, Art. 5, pages 541-720, July, 1954).... The 1954 and 1955 dates for examinations of the American Board of Psychiatry and Neurology are: Dec. 13 and 14, 1954 (New York City); Feb. 28 and March 1, 1955 (New Orleans); Oct. 17 and 18, 1955 (San Francisco); and Dec. 1955 (New York City).

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NEW REPORT CONFIRMS VALUE OF PARSIDOL IN TREATMENT OF PARKINSON'S DISDEASE

According to Dr. Harold Berris, writing in the July issue of THE JOURNAL-LANCET, 8 of 14 patients were helped by Parsidol, a new drug for the treatment of Parkinson's disease. He says: "In many of these patients reduction of the tremor was so definite that many of the self-care activities were greatly facilitated. Several of these patients, because of the reduction of tremor, were now able to shave themselves, light their own cigarettes and in general carry out a number of functions which were impossible while on other medication. . . . The drug appears to be relatively non-toxic." Of the remaining six patients two felt no change and four thought that they were better on previous medication "even though objectively no definite difference could be observed," the doctor noted.

Parsidol was made available in the United States for the first time earlier this year by Warner-Chilcott Laboratories, New York City and Morris Plains, New Jersey, the pharmaceutical division of Warner-Hudnut, following encouraging clinical reports of its use against Parkinson's in this country and in England, France and New Zealand. Of the eight patients in Dr. Berris' study who benefited four were on Parsidol alone and four were receiving the agent as an adjunct to other drugs. The patients' ages ranged from 22 to 78. In addition to controlling tremor, Parsidol also relieved muscle rigidity.

ALLIGATORS EMPLOYED IN TESTS OF DIAMOX, NEW LEDERLE DIURETIC

The alligator is proving a useful animal for medical research as well as a source of leather for purses, belts and shoes. According to a report in Science, Thomas Hernandez and Roland A. Coulson of the Louisiana State University's department of biochemistry used Mississippi river alligators to study the effects of Diamox, the new oral nonmercurial diuretic developed by Lederle Laboratories. Several alligators with an average weight of about 1.5 kilograms were used in the experiments of the New Orleans investigators.

While the drug had a diuretic action in the alligators, it was found to be "feeble" in comparison with its effects in the dog, man, rat and fresh-water catfish. The alligator has an unusual kidney structure and the composition of its urine is different from that of mammals.

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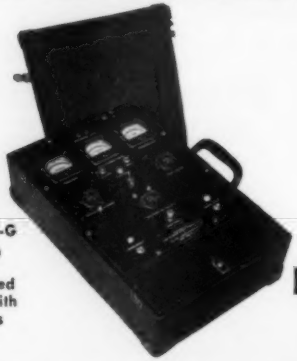

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2. Berris, Harold: *Neurology*, 4:116, Feb., 1954.
3. Carter, Sidney, and Merritt, H. H.: *Am. Pract. & Digest Treat.*, 3:547, July, 1952.

Mebaral, trademark reg. U.S. Pat. Off., brand of mephobarbital